The Canadian Medical Association Journal

Vol. 48 TORONTO, JUNE, 1943 No. 6

THE SURVIVAL OF PRESERVED ERYTHROCYTES AFTER TRANSFUSION*

By O. F. Denstedt, B.Sc., Ph.D., Dorothy E. Osborne, B.Sc., Dr.-es-Sci., H. Stansfield, M.D., M.Sc. and I. Rochlin, M.Sc.

Department of Biochemistry, McGill University, Montreal

THE capacity of preserved red cells to remain in circulation after transfusion is the only reliable criterion of their physiological worth, and is the only basis on which methods of preservation can be evaluated. It is assumed, of course, that all red cells in circulation are functional and that they are removed as soon as their physiological properties are seriously impaired.

For estimating the number of transfused cells in circulation there are two methods. In one, introduced by Ashby[1] in 1919, blood from a group O donor is transfused into a subject of group A or group B. Periodically thereafter small samples of blood are taken and the recipient's cells are selectively agglutinated with an appropriate serum leaving the donor's cells free to be counted. The second method, introduced by Wiener[2] in 1934, is similar in principle but makes use of the M and N blood types. Cells from a donor OM are transfused into a subject of group ON, or vice versa, and in periodic tests the recipient's cells are agglutinated with a suitable anti-serum prepared by immunizing rabbits against human OM or ON cells. The latter method is preferable, being less liable to interference from other factors. The two procedures when used concomitantly, however, give close agreement.[5]

Wiener and Schaefer[3, 4] were the first to apply the MN method for following the survival of preserved cells after transfusion. They observed that after transfusion of citrated fresh blood or specimens stored for only a few days, the cells could be detected in the circulation for three or four months, while cells (blood) that had been stored for longer periods disappeared more rapidly. These investigators concluded that for blood stored in citrate alone at 4° C., the time-limit of preservation is from 7 to 10 days, an observation since confirmed by many other workers.

With the steady improvement in preservation methods the period of useful storage has been considerably extended. Preservative mixtures have been improved chiefly by the addition of dextrose and the adjustment of salt concentration and the proportion of blood to diluent. Cell-survival tests reported by numerous investigators[5 to 13] during the past three years have established that red cells stored up to 14 days, and in some instances 18 days, survive as well as fresh cells after transfusion. If stored for longer periods an increasing number of cells suffer deterioration, hence when placed in circulation again are more rapidly removed. Even with 30-day-old blood, however, the rate of cell removal is not very rapid, and in emergencies these and even older specimens have been used with good results in the treatment of severe blood loss.

In the operation of blood-banks and in research on cell preservation, it would be very helpful to have a method for ascertaining the condition of preserved samples without transfusion. Numerous tests have been tried but have been found of little value. The estimation of free hæmoglobin in stored specimens, for example, is of little practical use since, with improved methods of preservation, blood can be stored for 35 or 40 days with less than 1% hæmolysis. The deteriorative changes, which limit cell survival on the other hand, set in about the 20th day and are far advanced by the time cell breakdown begins.

The fragility test is of still less value for estimating the condition of preserved cells. Mollison and Young[7] have shown, and the present writers have confirmed, that there is no correlation between the stability of cells to hypo- and isotonic saline solutions and their

* As part of a general investigation on the preservation of blood, assigned and supported by the National Research Council of Canada.

capacity to survive after transfusion. Usually the survival is much better than the fragility test indicates. The discrepancy may be explained in part by the circumstance that when preserved cells are placed in the blood stream or even in contact with fresh plasma for an hour, the normal stability to salt solutions is restored.[7, 15] Maizels[9] has observed, furthermore, that transfused cells become reconditioned with respect to electrolyte content and that they recover their normal composition within 24 hours. Whether other autolytic changes during storage also are corrected after transfusion, is not known. If this does occur to any extent it doubtless takes place to a greater degree in some cells—presumably the more normal ones—than in others.

Greater success has been achieved in preventing hæmolysis during storage than in retarding the autolytic changes inside the cell. Despite the extension of the period of cell preservation to 35 or 40 days, stored cells cease to be equivalent to fresh cells after the 15th or 20th day as judged by the capacity of the cells to survive after transfusion. It may be inferred either that little change occurs in the cells within this period, or what seems more likely, that the changes are reversible after transfusion. After the 20th day the reversibility is less complete and as a result the longevity of the cells is diminished.

PRESERVATIVES

The purpose of the present investigation was to determine the merits of two preservative mixtures which have given excellent results as judged by the prevention of hæmolysis during storage, and the stability of the cells when placed in sterile compatible plasma for 4 hours at 25° C. The mixtures were developed during 1940 and 1941 as a result of a comparative study on the preservative solutions reported in the literature up to that time. The one solution, a citrate-dextrose mixture described in a previous report,[14] is a modification of DeGowin's preservative, the difference being that the amount of isotonic dextrose is reduced to make the ratio of blood to diluent 1:½. Further reduction to give a 1:⅓ ratio affords practically as good preservation of red cells, but favours more rapid precipitation of fibrin during storage. The second preservative, consisting of isotonic citrate-dextrose buffered at pH 7.4 with isotonic phosphate, resulted from experiments with sodium metaphosphate, which has been recommended by Olef[16] for the preservation of erythrocytes, white cells and platelets for serological purposes. In later experiments it was found that the more physiological orthophosphate is equally effective as a preservative for red cells.

While the buffered mixture, with the majority of bloods, is superior to citrate-dextrose in retarding hæmolysis, its chief merits are in retarding cell swelling during storage, and in reducing the packing and cohesion of the cells on sedimentation. It is difficult to say whether the observed reduction in fibrin precipitation in many of the buffered specimens was attributable to the influence of phosphate. The merits of the two solutions with respect to the preservation of the functional properties of the cells were tested by cell survival after transfusion.

EXPERIMENTAL

Selection of subjects. — The cell-survival studies to be described were carried out at the Verdun Protestant Hospital (Mental) at Verdun, Quebec. Wassermann-negative male subjects chiefly of groups OM and ON were selected, whose weight records during the previous two years had been fairly constant. One patient with severe pernicious anæmia, who required transfusion, was included. Except in this one case, the general procedure was to remove 400 c.c. of blood for storage, and immediately to replace it with a transfusion of 600 c.c. of preserved mixture (containing 400 c.c. of blood). Three subjects, including the anæmic patient, exhibited an abnormal tendency to eliminate donor cells and therefore were given a second transfusion after the first cells had disappeared in order to determine whether the rapid elimination was characteristic of the recipient or whether it was attributable to some property of the donor cells.

Preservation of samples.—Blood was donated by students of McGill University as well as by the patients who received transfusions. The preservative mixtures and storage methods are described below.

1. *Isotonic citrate-dextrose.* — (1) Sodium citrate—3.2% solution of the dihydric salt. (2) Dextrose—5.4% solution of C.P. anhydrous dextrose. These were used with blood in the following proportions: Blood, 400 c.c., citrate, 80 c.c., dextrose, 120 c.c.

2. *Isotonic buffered citrate dextrose.*—(1) Iso-

tonic sodium citrate (3.2%). (2) Isotonic dextrose (5.4%). (3) Isotonic phosphate buffer pH 7.4 prepared as follows: 0.3 molar (4.14%) $NaH_2PO_4.H_2O$ (monobasic sodium phosphate) 1,000 c.c.; 0.3 molar (1.2%) NaOH (sodium hydroxide) 925 c.c.; water 480 c.c.

These solutions were autoclaved separately and mixed when cool. Blood and the preservative mixture were used in the following proportions: Blood, 400 c.c., citrate, 80 c.c., buffer, 40 c.c., dextrose, 80 c.c. Fresh, twice-distilled water was used in all solutions and they were sterilized without delay.

In addition to the above two mixtures, DeGowin's formula was used with three stored specimens as follows: Blood, 200 c.c., citrate, 40 c.c., dextrose, 260 c.c.

In some instances the preservative solutions were equilibrated with carbon dioxide by placing the containers, with the tops well protected with a thick cotton pad, in a desiccator which then was evacuated and filled with carbon dioxide. Blood was collected into chilled preservative solution without the aid of aspiration and by the method previously described.[14] The specimens were stored at 4° ± 1° C.

Agglutinating serum.—Potent anti-M and -N sera were prepared in our laboratory according to the method of Wiener.[17] The unabsorbed sera were stored at about 0° C. Sufficient serum for each experiment was absorbed a few days prior to the transfusion and in several instances the material was given a final absorption with a small quantity of the prospective donor's cells. The final product was dispensed in 1 c.c. lots in sterile serological tubes and was stored either in the frozen or in the dry state. In the latter condition the potency is retained indefinitely. The dried material was reconstituted with distilled water to which a small amount of saline was added to make it slightly hypertonic. The frozen serum also retained its potency. A non-agglutinable count below 50,000 cells per $mm.^3$ with the recipient's blood was considered satisfactory.

Tests preparatory to transfusion. — The amount of free hæmoglobin in the plasma of the older stored specimens was estimated by a modification of the micro-method of Wu[18] or by that of Flink and Watson.[19] A stability test also was done using sterile compatible plasma as the test solution. One-fifth of a c.c. of the preserved blood was mixed with 2 c.c. of compatible plasma and after standing at 25° C. for 4 hours, the additional free hæmoglobin was estimated. The purpose of the test was to detect any instability and to correlate the amount of breakdown with the recipient's plasma bilirubin after transfusion. The authors have observed that with some preservative mixtures the red cells after resuspension, undergo progressive breakdown on standing at room temperature. Similar hæmolysis occurs if the cells are mixed with compatible plasma. With the preservative solutions used in the present study cell breakdown subsequent to resuspension is usually extremely small—even up to 24 hours.

Transfusion of blood and collection of test specimens.—Care was taken to ensure complete suspension of red cells by slowly swirling the preserved sample for from 5 to 10 minutes. The temperature was usually raised to about 10° C. in the process. Four hundred c.c. of blood and an additional 5 c.c. sample having been removed from the subject in the meantime, the preserved blood was administered without further warming. The transfusion usually was preceded and followed by a small infusion (50 c.c.) of saline dextrose from a saline tube connected with the system by a Y-tube. Immediately following the transfusion, another 5 c.c. sample of blood was collected into exactly 1 c.c. of citrate in a graduated centrifuge tube so that the degree of dilution could be accurately determined.

In all, 35 transfusions were performed, using blood ranging from fresh to 2 months old. No reactions were encountered. Three subjects received a second transfusion. All patients were very co-operative.

For subsequent cell-survival counts, small samples of blood were collected in citrate as described above, at the 4th, 12th and 24th hour, the 3rd and 6th day and thereafter at weekly or 10-day intervals. Free hæmoglobin and plasma bilirubin were determined by the methods of Evelyn[20, 21] on the 4-hour sample after transfusion of the older preserved specimens.

Estimation of circulating donor cells.—In mixing the test sample care was taken to avoid frothing. Blood was drawn up to the 0.5 mark in a white-cell pipette and then diluted to the 1.1 mark with isotonic saline. After mixing the contents the suspension was transferred to a small tube. With a dry pipette the dilute cell suspension was drawn up to the 0.1 mark followed by agglutinating serum to the 1.1 mark. The contents were then transferred to a small serological tube. A duplicate was prepared in the same manner from the first cell suspension. To avoid temperature effects all solutions were adjusted to 25° C. at the start. The tubes in duplicate were agitated for 3 hours on a shaker vibrating horizontally at the rate of 4 per second

and making an excursion of ⅛ inch. They then were flicked a few times by hand and a portion of the supernatant liquid was transferred to a hæmocytometer chamber. The free cells in a total area represented by 12 x 12 large squares were counted and the number of cells per mm.³ was calculated as follows:

$$\text{Total free cells per mm.}^3 = \frac{\text{Total count} \times 11 \times 22 \times 10 \times \text{Original vol. citrated sample}}{9 \qquad \text{Vol. of blood in sample}}$$

The cell-counts were checked by different individuals in most cases. The recipient's free-cell count was deducted in each case.

If the counts on duplicate tubes differed by more than 20% the tests were repeated in duplicate from the beginning. The experiment was continued until the survival curve reached the recipient's free-cell count, or until it flattened out at a low level.

Two methods are used in the following section for presenting the experimental results:

1. The highest count (per mm.³)—usually obtained at the 4th hour after transfusion, is taken as the basic figure and subsequent counts are calculated as percentage of the highest count. This treatment obviously disregards any removal of cells that may have occurred during transfusion or up to the 4th hour.

2. Since the expected maximum count cannot be determined without knowing the blood volume of the subject a count of 400,000 per mm.³ is an approximation of the value expected on the basis of body weight and amount of blood transfused. Taking this value or higher counts as the basic figure subsequent counts are expressed as percentage. This method, in a rough way, corrects for cells removed during transfusion. That some cells are disposed of at that time is indicated by the relatively low initial counts following transfusion of many of the older samples.

RESULTS

Condition of preserved specimens.—All specimens were in excellent condition from the standpoint of red-cell preservation. Even in the oldest samples hæmolysis was negligible (see Table III). All samples also were very stable by the plasma test described. Resuspension of cells was most easily accomplished in the buffered specimens and least readily in the most dilute samples.

Fibrin precipitation displayed the usual variability. Although the amount of fibrin increases with duration of storage, the rate of formation in different specimens varies so much that comparison is impossible. In the majority of samples after resuspension of the cells, the fibrin existed in very finely divided form. In a few cases a small, compact lump of white fibrin was observed surrounding the air-inlet tube. Except in one specimen in which complete dispersion of red cells was difficult all samples were administered without difficulty, using Baxter equipment with the regular 200-mesh-per-inch stainless steel filter. The single sample referred to above was used in case 20 (Table II) with good results.

There was no evidence that the storage of blood under carbon dioxide, recommended by some workers,[24] resulted in consistently better cell preservation or survival.

The survival of red cells after transfusion is represented in the graphs in Fig. 1, the hard lines indicating the percentage survival based on the highest count. In cases where the maximum was considerably below 400,000 per mm.³ the broken lines represent survival calculated on the basis of 400,000 as the expected maximum.

In Tables I and II the numbers in the first column correspond with the numbers of the curves in Fig. 1. The survival data in Table II are based on the solid curves. Since many of the curves exhibit discontinuities, the area under the curve at different intervals has been included as an index of survival and function for purposes of comparison.

Table III gives information pertaining to the amount of hæmolysis in the older samples and the recipients' plasma bilirubin after transfusion. The bilirubin value usually reaches a peak at about the 4th hour. All the stored specimens were very stable by the plasma test. Fragility tests on the older samples showed no correlation with cell survival.

DISCUSSION

When considering the behaviour of erythrocytes during storage or after transfusion it is well to bear in mind the statistical nature of the problem. In many respects the red cells in the blood stream are analogous to a population of people ranging from young to old, and in physical condition, from hardy to frail. At certain times the entire population is subjected to greater stress than at others. Each cell therefore has a life expectancy which depends on age, wear and tear, hæmolytic hazards and other factors. Some cells perish prematurely while a few may survive 125 days or longer. The average life-span is supposed to be about 80 days. When considering the fate of preserved cells after transfusion additional factors must be taken into account, namely, the effects of storage and the influence of the new environment, *i.e.*, the recipient. It is apparent, therefore, that the possibility of variation in results is very great, and that an accurate interpretation of results can be made only from a large number of comparable experiments.

It will be observed that some of the survival curves in Fig. 1, particularly numbers 1, 2, 14 and 16, are very irregular. At first it was suspected that faulty agglutinating and counting

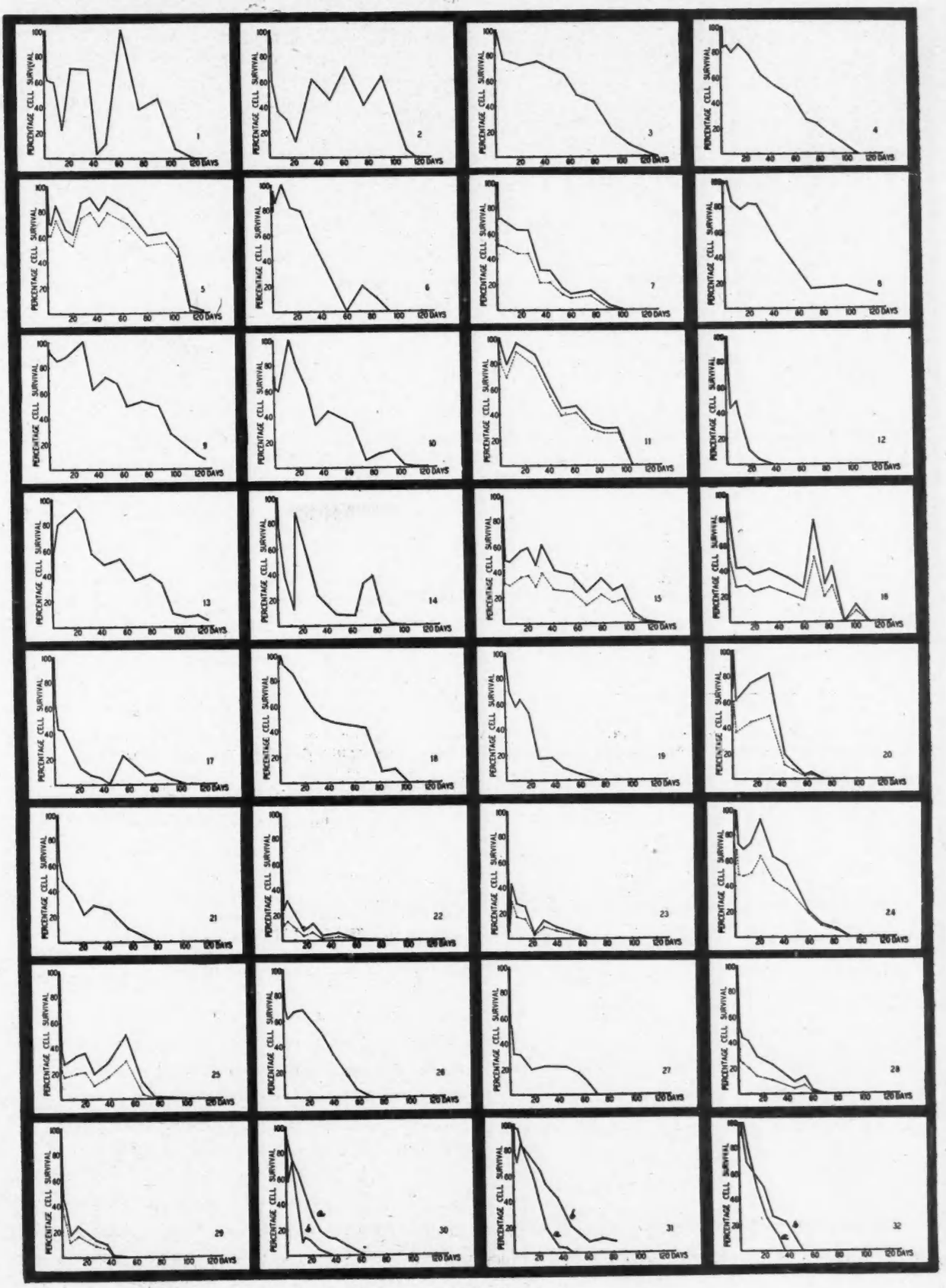
PERCENTAGE CELL SURVIVAL
20 40 60 80 100 120 DAYS
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Fig. 1

TABLE I.

	Recipient				*Donor*		*Transfused Sample*		
No.	*Age*	*Weight*	*Group*	*Condition**	*Age*	*Number†*	*Days duration of storage*	*Grm. % Hb in sample*	*Preservative‡*
1	38	159	ON	E	36	2	Fresh		C.D.
2	36	152	OM	S	38	1	Fresh		C.D.
3	32	245 (obese)	ON	E.D.	30	A	1	Fresh	C.D.P.CO_2
4	59	130	ON	S.s.	41	12	14		C.D.P.
5	23	145	OM	E	34	B	15	10.0	C.D.
6	50	143	ON	M.d.	35	C	19	7.2	C.DI.
7	36	150	OMN	S.D.c.	25	D	20	11.2	C.D.P.CO_2
8	52	175	OM	P.S.	19	25	21	12.4	C.D.P.CO_2
9	20	139	ON	S.s.	56	20	22	11.6	C.D.P.CO_2
10	41	161	OMN	S.D.	50	29	23	11.7	C.D.P.CO_2
11	20	139	ON	Ps.	38	28	23	10.6	C.D.P.CO_2
12	53	135	OMN	S.s.	25	E	24		C.D.I.
13	26	163	OM	S.s.	25	F	24	11.6	C.D.
14	41	130	OM	S.	32	3	24		C.D.
15	48	143	ON	S.D.	30	A	24	10.9	C.D.
16	45	149	OM	F	20	11	24		C.D.
17	45	140	OM	S.	52	8	25	9.1	C.D.P.CO_2
18	43	146	OMN	S.	32	31	26	11.8	C.D.P.CO_2
19	26	145	ON	S.	26	G	27	11.3	C.D.
20	56	159	ON	M.d.	48	15	27	10.0	C.D.P.
21	50	132	OMN	S.	20	H	30	8.0	C.D.I.
22	40	145	OMN	S.D.	20	11	32	10.0	C.D.CO_2
23	38	160	ON	S.s.	20	9	32	10.6	C.D.P.CO_2
24	41	165	ON	S.	25	I	35	10.3	C.D.P.
25	19	139	OM	I	25	J	35		C.D.P.
26	49	133	ON	S.s.	25	K	39	10.6	C.D.P.
27	50	130	ON	P.S.	25	L	41	9.5	C.D.
28	38	157	OM	P.e.l.	21	M	42	11.6	C.D.P.
29	50	126	OM	S.D.	25	N	57	9.6	C.D.P.
30 (a)	57	166	OMN	M.d.A	45	17	3	Fresh	C.D.P.CO_2
30 (b)				AT	30	A	16		C.D.P.CO_2
31 (a)	32	135	OM	S.s.	49	26	19	12.4	C.D.P.
31 (b)					32	0	21	8.8	C.D.P.CO_2
32 (a)	34	168	OM	S.s.	56	27	22	9.5	C.D.P.CO_2
(b)					34	B	22		C.D.P.CO_2

Legend.

*A—pernicious anæmia; c—catatonic; D—deteriorated; d—depressive; E—epileptic; F—feeble-minded; I—imbecile; M—maniac; P—paranoid; P.e.l.—postencephalitis lethargica; Ps—psychopath; S—schizophrenic; s—simple; T—after a course of liver treatment.

†Letters denote normal donors, all of whom were male except donor M. Numerals refer to the subjects enumerated in the first column.

‡C—citrate; D—dextrose; P—phosphate buffer; I—DeGowin's mixture; CO_2—under carbon dioxide.

technique was the cause of the fluctuations, but this was ruled out by repeated tests. Curves 7, 9, 10, 13 and 15 also are somewhat irregular, but all show a fairly steady trend. If the irregularities be disregarded the majority of points will be found to lie on a smooth curve (not drawn). The regularity of the remaining curves in Fig. 1 is evidence of the reliability of the technique used and authenticates the irregular results referred to above. As regards testing-sera it is the writers' experience that if the material is carefully prepared and properly stored, its agglutinating properties remain constant. It is noteworthy, however, that the rate of agglutination of different bloods with sera of equal potency is not always the same. In the present study it was considered advisable to use sera of comparable potency, preferably not too strong, so as to avoid occlusion of free cells among rapidly agglutinating masses. A large excess of serum was used to ensure maximal precipitation of the recipient's cells.

If body weight is taken as a basis for estimating plasma volume the expected donor cell count after transfusion of 600 c.c. of preserved blood under the conditions of our experiments should range from about 490,000 per mm.^{3} for a 130-pound man to 360,000 for a 165-pound subject. Unfortunately, accurate cell counts on the transfused specimens were not done in all cases, hence it was impossible to calculate the expected counts. While the majority of initial values were of the order expected, there is no clear-cut relationship between them and the body weights of the recipients.

TABLE II.

Recipient Number	*Recipient's hæmoglobin grm. %	Highest free cell count after transfusion	Duration of storage of specimen Days	Percentage cell survival and area under the curve at the end of the following periods (days)									Area	Total Area	Donor cells detectable for — days
				3	7	10	15	20	25	**Area	30	50			
1	15.4	240,000	Fresh	57	36	34	27	15	27	*35*	45	46	*91*	*200*	120
2	13.7	267,000	"	62	59	45	27	64	70	*52*	70	12	*79*	*198*	120
3	16.2	420,000	1	90	77	75	74	72	73	*77*	75	68	*150*	*242*	130
4	15.5	420,000	14	85	80	82	86	80	75	*83*	65	50	*141*	*197*	110
5	16.3	345,000	15	70	85	77	66	63	77	*73*	87	85	*157*	*325*	130
6	16.5	253,000	19	85	95	95	82	80	75	*86*	60	41	*129*	*147*	95
7	14.8	282,000	20	72	69	67	63	62	62	*67*	45	20	*101*	*122*	100
8	14.2	465,000	21	99	83	81	77	82	81	*86*	75	43	*139*	*201*	130
9	13.9	457,000	22	89	85	86	87	92	95	*91*	90	70	*171*	*284*	140
10	12.2	278,000	23	60	75	90	96	75	70	*77*	45	40	*122*	*158*	115
11	16.5	355,000	23	90	80	87	96	93	90	*91*	86	48	*148*	*221*	105
12	15.1	192,000	24	44	47	40	21	9	5	*34*	2	0	*28*	*35*	35
13	15.7	393,000	24	70	85	90	87	90	85	*83*	65	51	*139*	*228*	130
14	16.0	297,000	24	65	35	22	87	70	50	*53*	30	8	*72*	*102*	105
15	15.3	253,000	24	50	50	52	56	59	46	*51*	57	39	*100*	*163*	125
16	16.8	411,000	24	65	42	42	42	37	39	*47*	41	32	*85*	*164*	115
17	16.2	366,000	25	44	43	35	30	15	10	*32*	7	10	*37*	*58*	105
18	15.1	371,000	26	95	90	86	79	70	62	*82*	55	47	*130*	*180*	105
19	16.7	365,000	27	70	67	60	60	46	22	*59*	17	8	*74*	*77*	74
20	15.3	239,000	27	61	66	68	74	78	83	*73*	64	10	*110*	*113*	75
21	15.0	184,000	30	55	45	41	34	24	25	*40*	28	17	*67*	*73*	75
22	15.0	192,000	32	27	25	20	12	15	27	*21*	17	4	*35*	*32*	65
23	15.2	258,000	32	30	27	26	25	7	7	*21*	11	6	*29*	*33*	65
24	15.6	271,000	35	99	69	71	77	92	80	*78*	65	40	*134*	*157*	90
25	15.1	236,000	35	37	30	31	34	35	25	*30*	22	50	*62*	*85*	90
26	16.4	455,000	39	70	65	67	68	62	57	*65*	50	20	*101*	*104*	75
27	13.5	245,000	41	32	32	29	22	20	22	*38*	22	20	*52*	*69*	70
28	15.5	196,000	42	45	42	37	29	26	24	*36*	21	12	*47*	*55*	70
29	14.8	270,000	57	38	17	21	22	19	15	*24*	12	0	*31*	*31*	45
30 (a)	6.8	550,000	3	82	70	62	47	32	22	*54*	16	6	*69*	*69*	60
30 (b)	14.5	384,000	16	65	55	30	14	10	5	*29*	4	0	*30*	*30*	30
31 (a)	17.1	384,000	19	97	85	75	61	42	25	*68*	17	0	*74*	*74*	45
31 (b)	16.4	509,000	21	71	84	80	72	66	55	*74*	48	17	*110*	*123*	90
32 (a)	16.7	325,000	22	100	76	65	45	30	20	*57*	12	0	*61*	*62*	35
32 (b)	16.0	372,000	22	85	66	62	55	45	30	*61*	25	0	*78*	*78*	50

*Normal taken as 15.6 grm. per hundred c.c. of blood.
**Area in cm.^{2} under the cell-survival curve up to the period indicated.

POSSIBLE RELEASE OF CELLS

One interesting feature common to many of the curves is the increase in cell count between the 12th and 20th days, and again in some instances about the 60th day. The increase is very pronounced in curves 8, 10, 13, 14, 20 and 24, and the tendency is detectable in the majority of cases in which blood stored up to 30 days was used. The flat regions in curves 1, 8, 11 and 21 between the 15th and 30th day suggest that the peak values were missed. The authenticity of the increased counts was confirmed by repeating the tests several times. Furthermore, similar discontinuities may be observed in the results obtained by Mollison and Young[5, 6, 8] and by other workers.[11, 12, 23] It appears, therefore, that all cells that disappear from circulation are not necessarily destroyed immediately, but that some of them are stored, possibly in the spleen. The increased cell volume of the preserved cells perhaps may cause many of them to be held in the capillary beds. Later, these are released gradually, starting about two weeks after transfusion and reaching a peak within a week or so. The increase is not accompanied by a rise in total cell count or in the hæmoglobin level. If our interpretation of the phenomenon is correct, it follows that the total number of existing donor cells prior to each peak on the curve, may possibly be higher but should never be lower than the peak value.

TABLE III.

Recipient number	Storage period of sample. Days	Total free hæmoglobin in sample. Grm.	Per cent of cells hæmolyzed	Bilirubin in patient's circulation 4 hours after transfusion. mgm. % (in plasma)
24	35	0.23	0.38	Normal
25	35	0.40	0.6	4.1
26	39	0.32	0.5	Normal
27	41	1.86	3.2	3.3
28	42	1.08	1.5	2.8
29	57	0.42	0.7	4.7

If a correction be made so as to include the stored cells the values for percentage survival and area under the curve would be considerably increased in many cases.

Whether a release of stored donor cells can be elicited by an injection of adrenalin or by removal of blood, has not been tested. Nor has any attempt been made in these experiments to correlate the increased counts with the reticulocyte count. That new cells, because of the immaturity of their agglutinogens, may be non-agglutinable and therefore be included in the free-cell count, as suggested by Isaacs,[22] is unlikely in view of the observations of Mollison and Young.[5]

The reappearance of donor cells after the curve reaches the base-line as in curves 6, 16, and 17 appears to be authentic, since this is suggested also by the results of other workers.[3]

From the numerous studies reported on red-cell survival it is safe to assume that cells stored up to 15 days and even longer survive as well as fresh cells in the circulation. Even with fresh bloods, however, there is considerable variability as may be seen in cases 1, 2 and 3 in Table II. In the first two instances blood was removed from each subject and transfused into the other without delay. The subsequent cell counts were extremely erratic although the duplicates on individual points on the curve agreed very well. The rather low initial counts suggest the removal of some of the cells during transfusion, a condition hardly expected considering that the blood samples were as fresh as possible. This is confirmed also by the subsequent increases in cell count. It will be observed that the corresponding curves 1 and 2 in Fig. 1 are lower than the normal curves 3, 4 and 5. The duration of survival, however, was normal.

The tendency of some individuals to eliminate transfused cells at an abnormally rapid rate is illustrated in cases 30, 31 and 32. To ascertain whether the disappearance of cells was due chiefly to a propensity of the recipient or to inferior quality of the donor cells a second transfusion from a different donor was given after the first cells had disappeared. The results indicate that these subjects destroyed donated cells very rapidly. The same probably is true of subject number 12. These observations may be contrasted with those in cases 3, 4, 5, 6, 7, 8 and 9 in which bloods stored for comparable period were used. It is interesting also to compare the survival in cases 3, 15 and 30b in which the transfused blood was obtained from donor A. The different rates of elimination, therefore, appear to be recipient characteristics. Patient number 30 with severe pernicious anæmia was placed on liver therapy at the 12th day. It is noteworthy that despite the rapid increase in his hæmoglobin there is no evidence that the new cells interfered in any way with the donor-cells disappearance curve. The removal of the second transfusion 30b was extremely rapid. In view of the observation of Ashby[15] and of others[23] that cell destruction in the pernicious anæmia patient is not abnormal, it is possible that the cell removal in subject 30 is not directly related to the anæmia but that it is simply a property of the individual as in the non-anæmic subjects 31 and 32.

In contrast to the above individuals, subjects 3, 18 and particularly numbers 24 and 26 appear to conserve donor cells. At the same time there is the possibility that the donor samples may have been of unusually high quality. It is of interest that the donor for subject number 18 was one of the three who eliminated cells very rapidly.

The reason for the high initial counts in 30a and 31b is not clear since the counts in 30b and 31a were of the order expected.

The relatively low bilirubin levels in the subjects who received older preserved specimens (see Table III) indicate that cell elimination even in subject 29 who received the 57-day-old blood, was gradual and easily tolerated. In subject 29 the bilirubin returned to normal within 3 days and in the other cases, within 24 hours. There was no sign of icterus in any of the patients and only in subject 28 was there any indication of free hæmoglobin in the circulation. A slight amount was detected in the 24-hour sample. Hæmoglobinuria was absent in all cases.

All subjects displayed the usual variation in hæmoglobin from day to day. The fluctuations showed no correlation with those in the donor cell counts. No effects of the transfusions were observed in the patients apart from the assertion of some of them that they felt greatly benefited.

CONCLUSIONS

Both the preservative mixtures tested in this investigation gave excellent cell preservation. Blood can be stored up to 2 months with neg-

ligible hæmolysis and without becoming toxic. The preservation of the functional properties of the cells also was very satisfactory, but these qualities as a rule become impaired after the 18th day of storage.

From the standpoint of keeping the cells physically intact during storage and in preventing swelling and dense packing, the buffered mixture is somewhat superior to the simple citrate-dextrose solution. There appears to be little difference in the two mixtures, however, with regard to the preservation of the physiological properties as judged by the survival of cells after transfusion. The citrate-dextrose mixture has been in use in the blood-bank at the Montreal General Hospital for over a year with satisfaction.

At the commencement of the investigation it was anticipated that there might be a difference in the blood of mental and normal subjects in regard to stability during storage and in survival after transfusion. Since apparently healthy recipients were selected a fair degree of uniformity was expected with regard to cell-destroying propensities in these individuals. The results of the experiments, however, indicate rather that the reverse was found. There was no marked difference in the behaviour of blood from normal and mental subjects during storage and after transfusion, but much of the variability observed appears to be due to the recipients. One would expect, therefore, that if a pooled specimen were divided and transfused into several subjects, the respective rates of cell removal might differ widely. The writers are inclined to think that this type of variation is more pronounced in mental subjects than in normals. The variability doubtless is accentuated by the deteriorated state of many of the individuals and by their confinement and inactivity.

It is impossible to state precisely how long preserved cells remain physiologically equivalent to fresh cells, in view of the variables involved. It might be said that as a rule red cells stored up to 18 or 20 days, by almost any of the improved methods, may be considered equivalent to fresh cells. Or more accurately stated, the probability that the survival curve of a preserved specimen will coincide with that of the average fresh specimen is high up to 18 days storage and decreases rapidly as the storage period exceeds this limit. This statement provides for anomalous cases such as number 13 in Table II where a 24-day-old sample gave better survival than the fresh samples in cases 1 and 2.

Since red cells stored up to 15 or 18 days usually show normal survival after transfusion it is reasonable to suppose that the changes in the cell membrane and in the non-diffusible organic compounds within the cell during storage, may be corrected after transfusion. This is in line with Maizel's observation[9] and is suggested furthermore, by the reversibility of the changes in certain of the organic phosphates during storage. It appears likely also, that after the 18th day the degree of reversibility in some of the changes is diminished, thus resulting in an increased rate of cell removal after transfusion.

If the areas under the curves be taken as measures of the general survival of the blood-samples transfused, there is little correlation with the period of storage; it is true that the three largest areas are obtained with bloods stored not exceeding 25 days, and that the three longest-stored bloods yielded areas much smaller than the average (both these points being statistically significant), but apart from these instances correlation is not observed. Even if it had been possible to calculate the expected initial count with accuracy and hence obtain more accurate "survival areas", there still would have been little correlation between the latter and the duration of storage.

In the practical application of preserved blood the important consideration is not how long transfused cells may be detected in the circulation, but what proportion of the cells remains during the period of greatest need. Even with 25- or 30-day-old samples a sufficient number of cells remain in circulation for 20 or 25 days to warrant using such specimens when whole blood is needed and when fresher samples are not available. The efficacy of month-old blood in the emergency treatment of severe blood loss has been demonstrated repeatedly in the present war.

SUMMARY

The purpose of the investigation was to determine the merits of two blood-preservative mixtures, the one, an unbuffered citrate-dextrose solution, and the other, buffered with phosphate at pH 7.4. Both mixtures were isotonic with normal plasma. Blood can be stored in these solutions up to 6 weeks or 2 months at 4° C.,

with less than 1% hæmolysis. The buffered solution gives slightly better cell preservation during storage and favours less dense packing of cells on sedimentation.

The survival of erythrocytes after transfusion was followed in 32 mental subjects by the MN method of Wiener. Specimens stored up to 2 months were used without any reaction. With regard to cell survival the buffered mixture did not exhibit special merit. The results of the study indicate that cells stored up to 18 days by either method survive as well as fresh cells after transfusion. Even with 25- or 30-day-old blood cell survival after transfusion is sufficiently high during the first three weeks to warrant the use of such specimens in the treatment of severe blood loss when fresher blood is not available.

There is evidence that some of the transfused cells may be stored instead of being destroyed, and that they are released into the circulation again between the 15th and 25th days. A second and less marked rise in donor-cell count often is observed about the 60th day.

The authors desire to thank Dr. C. A. Porteous, Medical Superintendent, and Dr. G. Reed, Assistant Medical Superintendent of the Verdun Protestant Hospital for facilitating this investigation, and Miss A. Lyford, R.N., Miss D. Keith, R.N., Mrs. Francis Adams, R.N., and Dr. R. Jones of the hospital staff for their assistance. We are grateful also to students of McGill University for donating blood.

We are indebted to Dr. P. Levine of the Beth Israel Hospital, Newark, N.J., for demonstrating the method of absorbing immune serum, for checking some of our test sera and for helpful advice.

Our thanks are due also to Miss MacNeil-Smith, and Mrs. D. Murphy for assistance in counting cells on numerous occasions, and to Mr. Thos. Ritchie for autoclaving service.

Acknowledgment is made also of helpful suggestions from Prof. D. L. Thomson and Prof. J. B. Collip.

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* The authors apologize to Drs. G. S. Schaefer and A. S. Wiener for the error in this paper.

VOLE ACID-FAST BACILLUS VACCINATION IN EXPERIMENTAL TUBERCULOSIS

By Dudley Irwin and D. C. O'Connell

Banting and Best Department of Medical Research, University of Toronto, Toronto

THIS paper reports the resistance against subsequent tuberculous infection developed in guinea pigs after injection of vaccines prepared from the vole acid-fast bacillus.

The vole *(Microtus agrestis)* is a small rodent which inhabits the fields of the British Isles, and is closely related to the field or meadow mouse of this continent. The vole is slightly larger than the common mouse and in appearance resembles a miniature muskrat both in colour and body proportions.

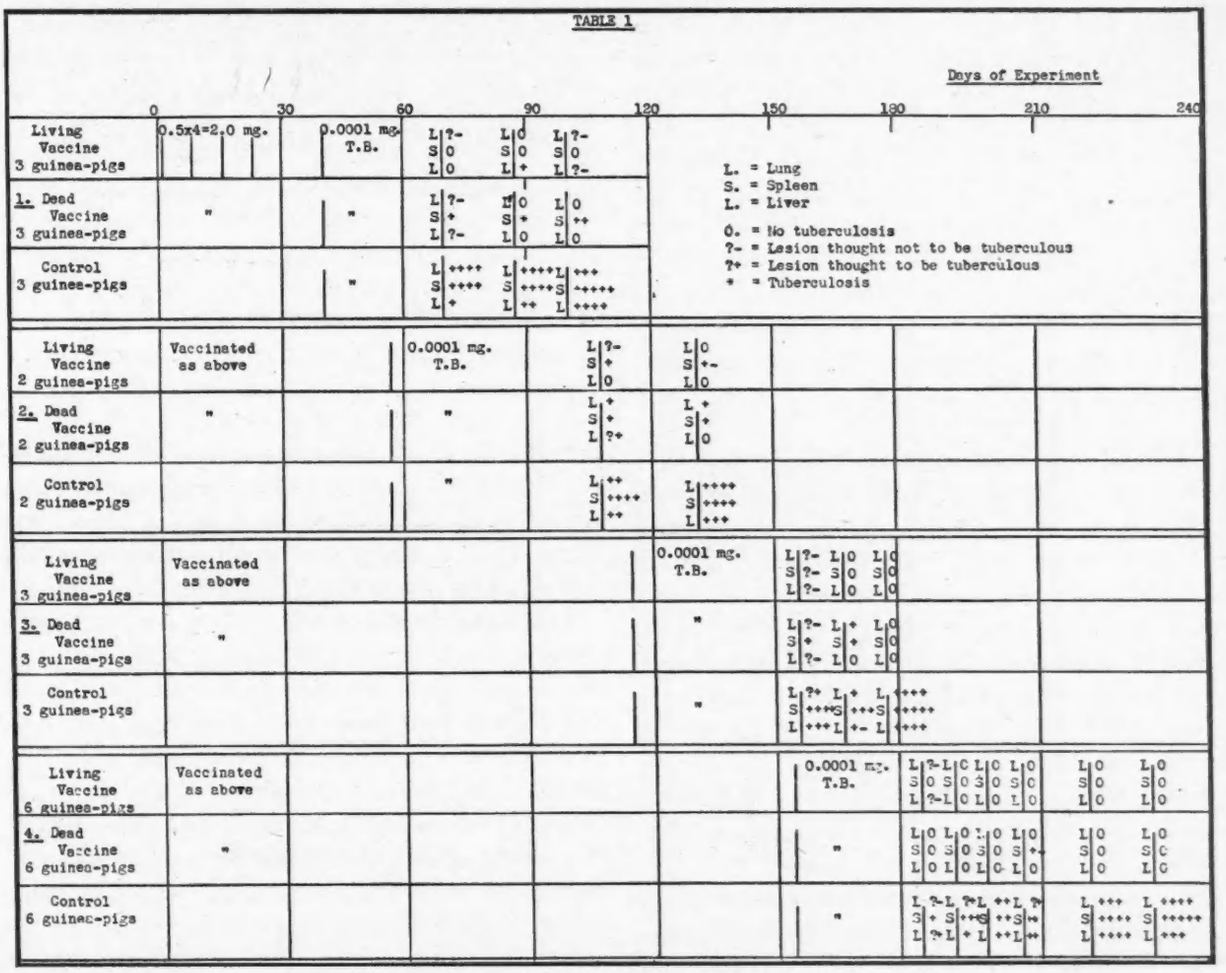
Fluctuation in the vole population of the British Isles had been studied for some years by Elton *et al.*,[1] and by Findlay and Middleton.[2] The vole population was found to rise each year, for three or four years, in a step-like manner, and then to fall suddenly, over a period of one or two months. The possibility of this sudden decrease being due to epidemic disease was investigated by Wells.[3] He found diseased voles with caseous areas distributed extensively throughout the subcutaneous tissues, lymphatic glands and lungs. The injection of this caseous material into healthy voles reproduced the disease and caused their death. An acid-fast bacillus was observed in and cultured from these lesions. The nature of the growth and the morphology of the organism were similar to those of the tubercle bacillus. With reservations, it was assumed that the vole infection was tuberculosis. Wells[4] subsequently determined that the vole was relatively susceptible to infection with the bovine and relatively unsusceptible to infection with the human strain of tubercle bacillus.

Subsequent investigations by Wells and Brooke[5] showed that the acid-fast vole bacillus is only slightly virulent for guinea pigs. They found that a large subcutaneous injection of the organism (5 mgm. +) might produce progressive disease and death while lesser amounts produced only a regressive local lesion. The same workers found that the vaccination of guinea pigs with the living acid-fast vole bacillus (4 doses of 0.5 mgm. at weekly intervals) gave, after an interval of five months, a degree of creased resistance to subsequent tuberculous infection. A culture of the vole acid-fast bacillus (L.V. 285) was obtained from Wells. This strain was isolated by Griffith from a naturally infected vole supplied to him by Wells.

Experimentation with this organism has been underway for some time and is continuing in this department.

The results of the initial experiments given below show the degree of resistance against experimental tuberculous infection that is pro-

TABLE 1



protection against experimental infection with the tubercle bacillus (0.000001 mgm. bovine or human types) "which apparently is far greater than has been produced by other means".

Griffith and Dalling[6] obtained similar results in calves. A subsequent study by Brooke[7] revealed that in all probability the vole acid-fast bacillus was a hitherto undescribed type of mammalian tubercle bacillus and he suggested the name of *Mycobacterium tuberculosis muris* (mouse).

The findings of these investigators offered a new and promising method of producing induced in guinea pigs by vaccines prepared from the vole acid-fast bacillus.

EXPERIMENTAL PROCEDURE

1. *Animals used.* — The animals used were young male and female adult guinea pigs, some albino and some of mixed colour.

2. *Vaccine preparation.*—Stock cultures of the vole bacillus were carried on a modified Loewenstein's medium. The organism for vaccine preparation was transferred from stock cultures through an egg yolk saline medium to a modified Petragnani's medium. The vaccines were pre-

pared by removing colonies of the organism from the surface of the medium, which after blotting between filter paper and weighing, were suspended in saline with the aid of glass beads. The concentration of the vaccine was 0.25 mgm. per c.c. The killed vaccine was prepared by heating to 60° C. for one hour. The vaccines were used the day of their preparation.

Animal Vaccination

Three groups of guinea pigs were used. The first was inoculated with living vaccine, the second with killed vaccine, while the third was used as a control group. The vaccine was injected subcutaneously in the lower abdomen each week for four weeks. Each vaccinated animal received a weekly dose of 0.5 mgm. or 2.0 mgm. in all. At four intervals after vaccination animals from each of the three groups were infected with the Johnstone strain of human tubercle bacillus by the subcutaneous injection in the groin of a saline suspension of 0.0001 mgm. (blotted weight) of the organism.

Findings

Animals from each of the four groups were sacrificed at intervals after infection with the tubercle bacillus. The extent and distribution of gross lesions were recorded at the time of autopsy. Tissue for section was taken routinely from the lungs, liver, spleen, and from lesions observed elsewhere. Such tissues were sectioned and stained both with hæmatoxylin and eosin and with carbol-fuchsin. The diagnosis of tuberculous lesions was based on the microscopic findings while the amount of the tuberculous reaction was based on the gross appearance at the time of autopsy.

The amount of tuberculous involvement in the lungs, spleen and liver is recorded for each animal in Table I along with the time relations between vaccination and infection and between infection and autopsy.

It will be seen from Table I that the control animals all showed tuberculous involvement which was extensive and severe six weeks after the experimental infection. All the animals vaccinated with the acid-fast vole bacillus showed less tuberculous involvement than did the corresponding controls. The severity of the tuberculous lesions in the vaccinated animals decreased as the interval between vaccination and experimental tuberculous infection increased. In the 4th group of animals in which experimental infection was not carried out until 18 weeks after the last dose of vaccine only one animal in twelve showed any tuberculous involvement. The results obtained in the vaccinated animals indicate that the killed vaccine was almost as effective in increasing the resistance of the guinea pigs to subsequent tuberculous infection as was the living vaccine.

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THE DIABETIC*

By Elliott P. Joslin, M.D., Sc.D.

Medical Director, George F. Baker Clinic, New England Deaconess Hospital, Boston

AS I look at this very youthful audience, seasoned with but few gray hairs, I am sure, President Cody, that my surmise was correct. You asked me to Toronto not to talk on diabetes because this group has been informed about that by those far more competent than I, in fact, by the leading instructors in the world in that subject; but rather to tell those assembled here about what they, being so young, know less and I, being old, ought to know more, namely, the diabetic.

Today it is difficult to find a Simon-pure diabetic. The patient one sees is a diabetic transformed and the characteristic symptoms of the disease are submerged. Therefore, without more ado I shall speak quite informally about some of the patients who have left a lasting impression on my life and have influenced me most in striving for better methods of treatment.

Mary Higgins was my first case. She was assigned to me as a clinical case to report upon before my classmates of the Harvard Medical School in 1893. Mary was then 26 years old and her diabetes developed that year. Already she had lost one-fifth of her body weight and her polyuria was such that she excreted the

* The Second Banting Memorial Lecture, delivered at the University of Toronto, on February 22, 1943.

equivalent of nearly one-fourth of her weight in cubic centimetres of urine in twenty-four hours. On one day the percentage of sugar reached 10 per cent, and on another the total quantity of sugar amounted to 535 grams; the urea reached 106 grams. Her eyesight varied from time to time. Her hair dropped out. Her flesh and strength melted away from her body and catamenia ceased in the presence of the excessive polyphagia, polydipsia, and polyuria. There was an odour of acetone to her breath, and with the help of the professor of chemistry I demonstrated acetone and diacetic acid. I had nothing to do with her medical care, but I see from my notes that she was given arsenic and cod liver oil, and, although I told my classmates that codeine and opium were the acknowledged leading remedies for diabetes I am glad to see that I argued against their employment. The next to the last paragraph of my paper has more significance now than it did then. It read as follows: "The pancreatic gland has been recommended and tried in this form of diabetes and will be further tested in this particular case. It has almost universally met with ill success, though in a few instances a slight amelioration in the condition of the patient has been produced." At that time, I had not read Pasteur's words "In making observations, chance helps the mind that is prepared." After all, pancreatic gland was not given and neither I nor any one of my classmates ever thought of making an extract of it, even for oral use.

Mary Higgins vanished from my sight and was one of the few cases I have not traced to their conclusion, but I did record that she had a temperature and a cough. In that epoch, you know, it was to tuberculosis that the majority of diabetics succumbed. From Mary Higgins I learned respect for diabetes and I saw the inadequacy of treatment of the diabetic.

During my house-officership at the Massachusetts General Hospital, no single outstanding case of diabetes comes before me, but rather a composite picture of perhaps a dozen diabetics who entered the hospital apparently in a fair degree of health, but who in the course of a few days became ill, seriously ill, often with a fatal termination. So impressed with this fact was I that soon after my subsequent year of study in Europe I personally examined the original record of each diabetic patient entering the hospital between 1824 and 1898, and Dr. R. H. Fitz was kind enough to summarize the data in a paper which we published together. Of the total number of 172 diabetics in that three-quarters of a century 27% failed to leave the hospital alive and even in the following period, 1898 to 1913, the hospital mortality rose to 28%. This shows what happened to the diabetic less than a generation ago. That statistical study plus what had actually been forced upon me during my intern days led to a valuable therapeutic hint, namely, that sudden or rapid changes, presumably dietetic changes, in the life of a diabetic were dangerous.

Case 2 was my uncle's wife, Aunt Helen. She had lost 41 pounds when her diabetes was discovered at 47 years of age in 1890. Under the care of the best practitioner in Worcester she lived until 1899. Glycosuria usually ranged from 6.4 to 9.6%. I remember only too well hearing about her trips to her doctor in Worcester, leaving the village full of hope and returning invariably in despair. If there was any drug which she did not take, it was not the doctor's fault, because I am sure he meant to give her the benefit of them all. Those nine years of constantly varying medication and steadily downward progress ending in coma made me thoroughly dissatisfied with what was done for the diabetic and the lack of its scientific approach.

While in Europe during 1897 and 1898 I was prepared to seek new ideas about the management of diabetics, but I do not remember to have seen a single case either in Vienna or Berlin. However, I used diabetes to learn the German language, because the German diabetic text contained so many words of Latin derivation that it was easy to follow. While there, I also became familiar with the work of both von Noorden and Naunyn. In the year following my return the opportunity came to test their methods with Case 8. Fortunately she was older than my first cases, had lost only 24 pounds from her maximum of 185, and although she showed 5.0% glycosuria she was free from polyuria. Simple limitation of the total diet and a gradually increasing limitation of carbohydrate resulted in a sugar-free urine in five days and from then on treatment was easy. It is true in the course of the next thirteen years she had many diabetic complications—a carbuncle, gall stones, intermittent claudication, hemiplegia, and, twice, pneu-

monia, but her diet never wavered one iota from its prescribed schedule and she died without coma, having lived longer with diabetes than her contemporaries without it. Case 8 thus set up a standard of diabetic treatment for me to follow. Thereafter with each new case I sought the same result and though it is not yet attained in youthful patients I do know that upwards of a thousand cases like hers have earned and received their medal "for prolonging life's span after the onset of diabetes—a scientific and moral victory".

Case 8 and Case 4, the latter a boy of fifteen years, with onset in 1897, led me to Strasbourg in 1900, where I met Naunyn, Minkowski, Decius Gerhardt, and Magnus-Levy who had a year before published his epoch-making monograph on "Die Oxy-Buttersäure".

Two cases of coma in the Naunyn clinic had recovered and, with Magnus-Levy's characteristic manner, not only did he utilize them, but studied seven other cases with a thoroughness which today has not been excelled. Nevertheless, it was years later before it began to dawn upon me that coma was not the ultimate end of diabetes and of the diabetic, but I did catch the idea that there was a possibility of its prevention.

My case 4, the 15-year old boy, however, steadily advanced in severity and despite my best endeavours his diabetes remained uncontrolled. Eventually he went into coma, and, inspired by Magnus-Levy's monograph, I spent three days and nights at his home. Needless to say, he died on the third day, despite the 95 grams of sodium bicarbonate which I gave, orally, rectally and intravenously, and I still remember his sigh of relief when he temporarily came out of unconsciousness and exclaimed how glad he was that he had only two arms. The quantity of acidosis measured in terms of oxybutyric acid extracted reached 153 grams in 24 hours, or, calculated by the difference between acids and bases, 180 grams. As a matter of fact, this was the greatest amount of oxybutyric acid up to that time ever exhibited in a case of diabetic coma. The nitrogen rose to 23 grams and the chlorine dropped to 1.2 grams in 24 hours. But, balancing the total acid obtained with the total alkali given, it was plain that such therapy would always be insufficient, and although a few cases of recovery from early coma had crept into the literature, such a method in an advanced case must inevitably fail. It was not until 1915 that I totally renounced alkalies and confined therapeutic measures in coma to the basic treatment of the disease diabetes and not the symptom, acidosis. Case 4 lived three years. Up to that time I had never seen a diabetic of his age who had lived so long.

My classmate, Case 351, who founded a well-known diabetic clinic in the West after he had developed the disease, always lives in my memory as the first case of severe acidosis I had the temerity to treat without the use of alkalies. Arriving in the early stages of coma, with the aid of bed rest, the help of a wonderfully trained nurse, the liberal use of liquids and salt, and starvation for three days, little by little he crept out of danger and lived usefully for many years. From that day, August 15, 1915, onward, none of my patients have received alkalies. With him, as with all patients, I have endeavoured to treat the diabetes first, believing the symptoms would then take care of themselves.

Diabetic coma took all the children. I remember a little girl whose Kussmaul respiration was so distressing that at the solicitation of the parents I promised to relieve it with medication and gave her a subcutaneous dose of morphine. Never again have I given morphine in coma. The relief was prompt, albeit startling to us all; respiration was paralyzed and life ended within a few minutes. Other dramatic examples come to mind: one was an old gentleman with appendicitis who was prepared for operation with morphine, but he breathed so slowly that an unusual quantity of ether was necessary to anæsthetize him. He, too, lived but a few hours. Here we had morphine and ether. Shortly after, occurred a more striking example of the effect of ether anæsthesia. A middle-aged woman, with two children, Case 729, whom I had treated for several years, went without my knowledge to a dentist in Malden on a Tuesday for dental extractions and for these was put under the influence of ether. She had nausea and vomiting on Wednesday, disorientation on Thursday, and died of coma on Friday. This was in 1915. The last case in this ether category was a pregnant diabetic, who also had eluded observation, although originally left in my charge, and had followed the directions of a mental healer. When admitted to a hospital near Boston in a precarious state her prompt delivery was judged necessary by her original physician and obstetrician and she too was given ether. She died, the

baby died, and the husband climbed the hill behind the hospital and shot himself. Thereupon, I published every single case of pregnancy in a diabetic I had ever seen and tried to tell why each one recovered or died, thus groping my way to some safer procedure of treatment. My associate, Priscilla White, is doing this again in a forthcoming numebr of *Endocrinology*, but her account, beginning with 1936, includes 125 cases with but one death and that a month or more after delivery, and the survival of 88% of the babies. She now has 31 undelivered pregnant diabetics under observation.

During 1913 Frederick M. Allen, who had worked laboriously upon diabetes in animals at the Harvard Medical School and had later gone to the Rockefeller Institute in New York, chanced to be in Boston and I showed him the record of a young bank president, Case 344, whose diabetes had lasted for some ten years, but with gradually increasing acidosis as evidenced by the secretion of 30 or 40 grams of B-oxybutyric acid daily for a year, and even rising on one occasion to 54.8 grams of oxybutyric in 24 hours. His diabetes changed abruptly and rather rapidly began to lose its severity. I could not understand this. Although the patient was growing sicker and sicker and losing more and more weight, due to the supervention of tuberculosis, his diabetes was progressively becoming milder. I told Dr. Allen if he could only explain this phenomenon, then he would have a key to the treatment of the diabetic. He pondered over it and the next day came back to my office and said he thought he knew the reason and would attempt to demonstrate it in animals. You know the rest of the story—the introduction of fasting and undernutrition.

Fasting, and one might just as well call it fasting as to call it by the gentler term "undernutrition", wrought radical changes in my patients. Profiting by Dr. Allen's suggestions, but remembering that early impression from my house-officer days at the Massachusetts General Hospital, I used fasting freely but gradually introduced it into the treatment of a case by the omission of fat the first day and then halving the carbohydrate and protein each following day until sugar freedom was obtained. Seldom did a patient fail to profit by the treatment, if measured by his becoming sugar-free; and the duration of life of my diabetics between 1914 and 1922 rose 25%, from 4.9 years to 6 years, so that there was no question of its usefulness. Little by little modifications occurred, and one saw, thanks to Newbugh and Petrén, that if the total calories were reduced and protein kept moderate, fasting might be avoided and considerable quantities of fat employed. It soon became evident from comparison of Petrén's and my cases that his adults did better with a restricted carbohydrate and high fat ration than did mine, whereas my children kept longer alive when undernutrition was carried to an extreme. Children really lived a considerable period of time, but life was not a joy and their aspect so pathetic that I remember how shocked Professor von Noorden was on his visit to Boston when he looked at one of my 14-year old diabetic girls, Case 2,256. Her emaciation was so extreme that he turned away in disapproval at the sight of her, but she survived and last winter after an interval of more than 23 years was earning her living, interrupting her work for a successful appendicitis operation.

The aspect of these children was truly dreadful. We literally starved child and adult with the faint hope that something new in treatment would appear. It was a Cyrano de Bergerac fight. It was no fun to starve a child to let him live. One professor of pædiatrics openly said he hoped he would never see another diabetic child. Miss Mudge, Case 1,542, whose weight had been 155 pounds, weighed 69 pounds. She lived next door to the hospital. She had not walked over a flight of stairs for nine months.

To me the only description that fits the diabetic scene at that time was written years before by the Prophet Ezekiel and if you will only put into Dr. Banting's mouth the words the Prophet wrote centuries ago you will realize what diabetics were like in 1922 and what he did for them. No words of mine can equal this description and in the hope that you will always remember EZEKIEL, XXXVII 1-10 as the Banting Chapter in the Bible, I will repeat it.

"The hand of the Lord was upon me, and carried me out in the spirit of the Lord, and set me down in the midst of the valley which was full of bones,

"And caused me to pass by them round about: and, behold, there were very many in the open valley; and, lo, they were very dry.

"And he said unto me, Son of man, can these bones live? And I answered, O Lord God, thou knowest.

"Again he said unto me, Prophesy upon these bones, and say unto them, O ye dry bones, hear the word of the Lord.

"Thus saith the Lord God unto these bones; Behold, I will cause breath to enter into you, and ye shall live:

"And I will lay sinews upon you, and will bring up flesh upon you, and cover you with skin, and put breath in you, and ye shall live; and ye shall know that I am the Lord.

"So I prophesied as I was commanded: and as I prophesied, there was a noise, and behold a shaking, and the bones came together, bone to his bone.

"And when I beheld, lo, the sinews and the flesh came up upon them, and the skin covered them above: but there was no breath in them.

"Then said he unto me, Prophesy unto the wind, prophesy, son of man, and say to the wind, Thus saith the Lord God; Come from the four winds, O breath, and breathe upon these slain, that they may live.

"So I prophesied as he commanded me, and the breath came into them, and they lived, and stood up upon their feet, an exceeding great army."

Much has been said and written about Sir Frederick Banting, but I prefer to let Ezekiel's vision stand as my estimate of the man and what he did.

It was while living in the midst of this valley of dry bones that I went to New Haven in the autumn of 1921 and heard Dr. Banting haltingly describe his experiments in association with the then medical student, C. H. Best, in the Laboratory of Physiology at the University of Toronto, and listened to Professor Macleod's favourable comments. At about that time I had seen 400 diabetic children, of whom 195 were dead. You can imagine the reaction which his talk caused, and when the following spring I received a telegram from the Eli Lilly Company that I was to be given insulin within a few weeks, you can realize that from thankfulness I did not want to sleep.

Miss Mudge, Case 1,542, and considered by me to be my severest diabetic, was my first to receive insulin and on August 7, 1922; she still lives and cares for her household, her diabetes now controlled after 26 years of the disease with 4 crystalline and 32 protamine zinc insulin units.

Case 632, a Canadian officer, who had reached for his rank the pinnacle of achievement, came down with severe diabetes at the beginning of the last war. This patient taught me, like Case 8, that accuracy in detail and rigid adherence to the Naunyn and Allen principles could control the disease. I remember how he fought it, and although barred from active participation at the front, he held important positions here in Canada. Following the war he travelled for six months in Europe and maintained his urine sugar-free on a diet seldom exceeding 30 grams of carbohydrate. How thankful I was that he lived to see insulin! I remember he remarked how altered the atmosphere was at the diabetic convalescent home. Before insulin the children were quiet, but when insulin arrived they made a noise. He lived his twenty years, yet not his full life expectancy, because upon him at the age of fifty "Phœbus Apollo shed his gentle darts", as he did "upon Phrontis, the son of Oneta, Menelaus' helmsman", who "dropped dead with the steering oar of the moving ship within his hands."

When I heard that I was to be supplied with insulin, I jotted in this little notebook the names of 29 patients who I thought should first receive it. Among them was Rexanne, Case 894. I remember her well. I hardly dared to bring her to the hospital, because although I had followed her diabetes for eight years from its onset at 1.5 years of age, I feared that any change in management might bring on acidosis and a fatal outcome. There was so little insulin available that at the solicitation of her parents and, I regret with my acquiescence, she remained at home over Christmas. Rexanne when five years old sold Liberty Bonds in Newport so that her father, who helped to lay the North Sea barrage in the late war and those with him, and her mother and her sisters, would be protected. She had lived longer than any child under my immediate care, and I remember showing her before a skeptical pædiatric society and having her sing and dance despite her fasting days, to show that a diabetic child could sometimes be happy. Rexanne survived Christmas, but never lived to have insulin. But I did bring back another child into the hospital. His parents said, "Do anything you want to Freddie, Dr. Joslin, you can't make him any worse". They brought him in on a cushion, but he left some weeks later carrying a gun on his shoulder and his little playmates met him on his homecoming with a drum and they paraded around the block in Somerville.

Case 2,383 you know well, because a few years following the onset of his diabetes in 1921 he received a Nobel prize, thus demonstrating to what heights a diabetic can attain. He still is a full professor of medicine and carrying more than a full schedule of work.

Of Dr. Banting's associate, Charles H. Best, few words are necessary, first, because you know what Banting thought of him, second, because it was Charles H. Best who by the part

he played in the discovery of insulin changed *ipso facto* the status of the medical student from that of student to that of investigator.

What did insulin do for my diabetics? First of all, it gave them hope, second, it gave them strength and resistance to complications of the disease; and, third, it gave them life. Here are just a few figures. Prior to insulin, the age at death of my diabetics was 44.5 years up to 1914 and only 46.7 years from 1914 to 1922. Today it is 64.8 years. Prior to insulin my fatal cases lived 4.9 years up to 1914, and 6 years up to 1922, but in the analysis ending a year ago they were living 14.3 years. What the life expectancy was in the former periods I do not know, but five years ago it was calculated for my diabetics by the Statistical Department of the Metropolitan Life Insurance Company, who have furnished practically all the statistical data I ever quote, and it had risen to two-thirds that of individuals of the same age and sex, and I suspect today is nearer 75%.

TABLE I.
DURATION OF LIFE AFTER ONSET OF DIABETES

Era		*Years*
Naunyn	1898–1914	4.9
Allen	1914–1922	6.1
Banting	1922–1936	
Early		8.1
Late		10.7
Hagedorn	1937–1942	
Early		12.5
Late		14.3

GEORGE F. BAKER CLINIC
(Compiled by the Metropolitan Life Insurance Company)

TABLE II.
6,596 FATAL CASES OF DIABETES
PER CENT DURATION UNDER OR OVER 20 YEARS

Era	*Less than five years Percentage*	*Twenty or more years Percentage*
Naunyn	66.8	1.8
Allen	55.9	3.1
Banting		
Early	40.5	4.9
Late	22.5	10.2
Hagedorn		
Early	15.0	14.4
Late	13.0	19.3

GEORGE F. BAKER CLINIC
(Compiled by the Metropolitan Life Insurance Company)

The change in the causes of death in diabetics is striking. Prior to my personal knowledge, and only recently on the continent of Europe, most diabetics died of tuberculosis. But at the beginning of this century the chief cause of death changed. Between 1898 and 1914, 64% of my cases succumbed to diabetic coma, but in the last analysis of 6,596 deaths of my patients who are scattered over various parts of the world, deaths from coma had fallen to 3.3%. Moreover since August 20, 1940 at the George F. Baker Clinic at the New England Deaconess Hospital, we have had about 5,000 diabetic admissions and among them were 78 successive cases of diabetic coma yet without mortality. Whether our methods in the treatment of coma are good or bad, and some think them bad, at least they set a standard by which other methods can be compared.

TABLE III.
PER CENT DIABETIC COMA DEATHS
AMONG 6,596 FATAL CASES

Era	*Preventable Coma deaths*
Naunyn	63.8
Allen	41.5
Banting	
Early	15.0
Late	5.0
Hagedorn	
Early	3.6
Late	3.3

(Compiled by the Metropolitan Life Insurance Company)

TABLE IV.
DIABETIC COMA

Curable
In 30 months, August, 1940, to February, 1943,
no deaths from diabetic coma
in 78 consecutive cases (5,000± diabetic admissions)
George F. Baker Clinic
New England Deaconess Hospital

ARTERIOSCLEROSIS IN DIABETES

Today diabetics die most commonly of arteriosclerosis. The figure reached 60% since 1937, and in 36% of all the cases the heart was the seat of the final illness. Deaths from arteriosclerosis in the lower extremities, and in particular from gangrene, I am happy to say, have fallen and I believe the significance of its decrease is far more important than generally appreciated. From recently compiled tables it is plain that not only has gangrene dropped nearly one-half in the two periods, but at the same time the duration of the disease before the patients developed it has advanced nearly one-half. And this is not all. The age of the patients with these vascular changes is considerably greater than formerly, thus throwing in the element of senile arteriosclerosis to add to that of diabetic arteriosclerosis.

Today we cannot hope to reduce coma mortality very materially, but these facts about the decrease in gangrene, its appearance later in the life history of the diabetic and after a longer duration of the disease before gangrene develops, show that we are making headway in the prevention of arteriosclerosis, and that is fundamental. Every honest day of diabetic treatment lived by a diabetic, you and I know, helps to defer the appearance of changes in his arteries and helps in the outlook of all the other diabetics in the world, because by so living he proves that he can be a useful citizen.

THE "CURE" OF DIABETES

Are any patients with diabetes cured? I shall never publish a case of a cured diabetic, because one must observe such a case for years and obviously I cannot live long enough for that. We have many hopeful cases under observation, but no cures are claimed.

The duration of life of diabetics cannot help advancing, because of contemporaneous discoveries in other branches of medicine. The decline in tuberculosis has influenced our cases, but the longer period of exposure due to the lengthening of life of the diabetic conceals the actual statistical gain. At one time it was true that one out of six of 52 of our cases of diabetic coma upon recovery developed tuberculosis within five years and eventually 29% succumbed to it. This no longer holds, because the vitality of the patients is so much greater and opportunities for exposure to the tubercle bacillus have decreased. So, too, with pneumonia. Obviously the 16% mortality from infections has been lowered by the sulfonamide drugs, and this is manifest not only in pneumonia but in surgical complications and in infections of the kidney. It is only a few years ago that these latter caused us unusual worry, especially in girls, and it is a fact that up to now one-half of our fatal cases in children with autopsy show infections of the kidney; I do not anticipate these figures will be maintained.

ROYALTIES ON INSULIN

The Insulin Committee of the University of Toronto is too modest. An erroneous idea spread abroad some years ago regarding the royalties which it received from insulin. Very few people really know the truth about the matter. I regret that the exact facts either have not appeared in print or have not been widely circulated, and for that reason I felt the truth should be included in this Memorial. The correct statement is that the Insulin Committee of the University of Toronto received royalties only for services rendered in connection with the supervision of the manufacture and the standardization of insulin. For a very short period this arrangement was extended to include export of insulin from various places in Europe, but the plan was soon stopped. With this exception, therefore, the policy has consistently been that no income was received where a service in supervision and standardization was not rendered. And again I think it should be said here that neither Banting, Best, nor any individual in Canada ever received any part of the amount collected. Whatever stipend they obtained came from University sources.

The war is teaching us all the value of co-ordination of effort between the Army, Navy and Air Corps. To this all agree, but co-ordination in the use of insulin, diet and exercise in the treatment of diabetes is just as essential. A survey of our cases in the hospital by our younger associates opened my eyes. Even with the most liberal interpretation of the degree of treatment of these patients, they agreed that not more than one-third of the diabetics we see were fairly well treated, one-third, moderately well treated, and one-third, actually poorly treated. Indeed, the conclusion finally reached by us all was that it is seldom that one sees a diabetic who is treated 90% as well as modern methods would make possible. Insulin is so good that doctors and patients take advantage of it disregarding diet and exercise. Insulin is so good that it covers up a multitude of therapeutic sins.

The discovery and manufacture of protamine zinc insulin by Professor H. C. Hagedorn in Copenhagen was a great comfort both to old and young, and particularly as modified by Drs. Scott and Fisher here in Toronto. Today practically all our diabetics receive their insulin before breakfast; approximately 80% of the children require both protamine zinc insulin and crystalline insulin, whereas 80% of the older diabetics are adequately controlled with protamine zinc insulin alone. In a survey of the 1,800 diabetic patients treated at the George F. Baker Clinic of the New England Deaconess Hospital during 1941 the total quantity of insulin utilized by our patients was highest in the age-period 15 to 24 years and from there

fell very gradually to the lowest quantity for those cases 75 years of age or over.

Insulin by no means has accomplished all it can. In coma there is little needed in addition to insulin except salt solution to combat dehydration, but this does not apply outside of coma. Insulin must be harnessed to diet and exercise to draw the load. We still do not utilize insulin to best advantage. If a patient enters in coma we get him sugar-free within twenty-four hours, but how often do we do that when a patient enters with heavy glycosuria? If it is safe to clear the glycosuria in coma in short order with insulin, it is certainly safe to clear it up as quickly outside of coma, and this should be done in order to shorten hospital stay both for the sake of the patient and to make hospital beds available for other cases. The war is driving us to make diabetic treatment more aggressive. Constantly we are discriminating among our patients, sending out those who can get along fairly well in order to make room for others who need treatment more. In addition, if a diabetic on his part does not take an interest in doing everything to improve while in the institution, his stay will be shortened. However, with all our intensive education of the patient, we must remember that some learn rapidly and some slowly, and not expect more from the individual than he is capable of performing. The Bible says forgive not seven times, but seventy times seven.

DIET IN DIABETES

A resurgence in the usefulness of diet in the treatment of diabetes is in the air. I notice this in the literature and in contact with patients and doctors. They demand that their diabetes shall be controlled. They do not accept the idea that the presence of sugar in the urine and, still more, in the blood can be overlooked. They know that such a state is not normal and they will not tolerate a regimen which neglects the control of their diabetes. The recent work of Newburgh with diet alone in the treatment of obese diabetics is an illustration in point of this added interest in diet, but it is driven home far more to me each day by patients who consult our group in order to get sugar-free.

Diet today is simplified and for our patients at the George F. Baker Clinic of the New England Deaconess Hospital during 1941 the average carbohydrate up to 15 years of age was 180 grams and from 75 years of age and over, 149 grams, the average carbohydrate for all the patients and all ages being 156 grams. With this quantity of carbohydrate the patients in our estimation appeared to be doing well and satisfied. We are not encouraged to depart materially from this allowance because of the constant upward trend of life and the diminution of complications.

The number of diabetics in the United States approaches 800,000 and I still believe by 1950 will reach 1,000,000, because diabetics are continuing to live so much longer and thus there will be many more alive at any one time, even though the number of new cases may not increase. Whether new cases will increase materially because diabetic women now become pregnant so much more frequently, I have my doubts. It is very rare to see a family with more than two children after diabetes was discovered either in the husband or wife.

The mortality from diabetes in the larger cities of the United States halted its upward curve in 1941 and the recent figures released by the Census Bureau confirm this change. In the entire country it fell to 25.4 per 100,000 that year, in contrast to 26.6 in 1940. I am sure that in all those regions where the mortality has been low, such as I found in Arizona, year by year it will rise and eventually approximate the figures for our larger cities. This one can predict, because, gradually, (*a*) the former low mortality due to a youthful population, (*b*) a census containing more males than females, (*c*) a low percentage of Jews, (*d*) inaccessibility to medical care, and (*e*) incomplete statistical reports, will be less and less marked as the population of the country as a whole becomes more uniform and the areas in question are less isolated. Thus, I found in Arizona from personal investigation that the number of cases of diabetes was approximately the same, allowing for age and sex incidence, as in the eastern states. Even among Indians it was relatively as high when all factors were taken into account.

As I look at the diabetic situation today, a great opportunity for improvement in treatment exists. Diabetics on the average when they die have had the disease only about fourteen years and the expectancy of the living still is limited to two-thirds or perhaps three-fourths that of the average individual for the

same age and sex. Many needless deaths should be prevented, and as for the life expectancy of diabetics not merely that should be prolonged but their working capacity while they are living preserved, and not so often as now should they become invalids for years before the end. I want to see diabetics die—healthy. Here is an army of a million in number, truly an opportunity for improvement of the diabetic on a large scale. The opportunity and the need therefore exist for united effort in their behalf.

Diabetics constitute a select group of people. On the whole I think it is true, as I have already said, that they are more intelligent than the average citizen, and it is well-known that they come from an upper rather than a lower strata of society. In this latter respect they form a sharp contrast to patients with tuberculosis. Poverty does not favour the development of diabetics. We observe the truth of this with diabetic children. We try to take into our diabetic summer camps the neediest children we can find. No child is refused for lack of money. The parents are sent a letter in the early spring, asking if their child would like to go to a camp and are requested to state whether they are in a position to pay anything or $1, $2, $3 or more up to $12 or $15 a week. Few, it is true, pay the upper limits, but nearly all pay something, and in fact the children actually contribute voluntarily about one-fifth of the total cost of the camp expenses.

A recent study of 73 of our diabetic children who have lived over 20 years with diabetes furnish confirmatory proof of what I have just said. Dr. H. E. Eisele, when associated with us, analyzed the reports of these cases and found that "the educational achievement of those who made up this series was probably the most striking feature brought out in the study. College was attended by 42% as compared with 7% of the population of the continental United States who are 21 or more years of age. We discovered that the positions attained in economic and social life were not materially different from those in a similar group of persons of this age who did not have diabetes."

Diabetics, more than patients with any other disease with which I am acquainted, realize the advantage of furthering the study of diabetes for themselves and their families, because they know, first, that diabetes is hereditary, and second, that research led to the discovery of insulin. In any campaign to improve the treatment of diabetes and promote scientific studies into its cause I feel sure that for each dollar donated, another dollar would be furnished by the diabetics themselves. As a matter of fact, for the $250,000 which was given by Mr. George F. Baker, Sr., for the George F. Baker Clinic, an additional $350,000 was secured to assure its maintenance from patients and their friends.

To my way of thinking, there are limitations for any plan designed for the help of diabetics. Progress in diabetic treatment is so rapid that any program for the disease should be constructed for a limited period, let us say at least for five but not more than for twenty years. Any study of diabetes in the laboratory should go hand in hand with the study and care of the patients in the wards so that all engaged in the investigation will bear in mind the humanitarian side of the question. I think that several diabetic units scattered about the country would be preferable to one single unit, because each unit would be a stimulating centre of activity to doctors and the laity in its own locality. Also by this means comparison can be made of the efficiency of the different units and independent research and diversification of effort would be encouraged. Each locality should contribute to the support of its own unit. At least a dozen different cities in Canada and the United States present possibilities for the creation or development of such centres of diabetic activity.

Insurance companies profit greatly from improvements in diabetic treatment, and therefore should take a vital interest in the disease. Diabetics are living nearly three times longer than prior to 1914 and, therefore, insurance companies are reaping the benefits. Most advantageously can they aid along statistical lines, because they have such admirable methods. It is because of the help I received from the Metropolitan Life Insurance Company that our own clinical material has been analyzed.

Education of the doctor who cares for the diabetic should go hand in hand with the education of the patient and each centre should try for both ends. If a doctor is educated in the treatment of diabetes the good accomplished lasts for his entire medical life and is passed on to successive groups of patients, whereas the

education of a patient seldom spreads beyond his immediate family and friends.

In the last few weeks at informal conferences with several gentlemen representing broad interests, I spoke of clinics or laboratories where research in diabetes is going on and advantageously could be encouraged. Of course I am interested in what we are doing at the George F. Baker Clinic, but far more than that I am interested for diabetics as a whole, and I frankly will state that if asked where, in my opinion, capital could be invested most wisely in the furtherance of the diabetic problem in the United States and Canada, I should place first of all the laboratory of Professor Charles H. Best in Toronto.

The creation of an individual responsibility in the diabetic has been and remains the keynote of treatment. If the diabetic is not imbued with the necessity, the desire, and the duty to maintain his health, there is little that a doctor can do for him. To a certain degree, I welcome this fact, because it will mean that the diabetics who live are the desirable diabetics, the good citizens. It is true that the career of careless and ignorant and despondent diabetics can be changed. To a large degree that is the responsibility of doctors and nurses, but over and above all the development of the soul of the diabetic and his zeal to be helpful goes along with the treatment of his body. But the fact remains that, no matter how we look upon it, the old adage holds, "You can lead a horse to water but you can't make him drink." By no means, however, am I oblivious of the responsibility which rests upon the doctors. No one feels this more than I. Doctors must officer this army of 800,000 souls. If their leadership fails, the army is defeated.

My ideal for the diabetic is a high one. Therefore, I dislike his seeking special privileges in the rationing of oil, gas, or even of food in addition to his release from war services. With the carbohydrate in the diet as high as 150 grams, the chances of a diabetic not being able to obtain enough calories in the form of protein and fat seem slight. For each ounce lacking in meat he can substitute fish, cheese, nuts, or an egg, and, unless rationing is instituted for chicken, duck, or turkey, he can fall back on poultry, and, besides, as yet there is no rationing of organs of animals, such as tripe, sweetbreads, kidneys, or liver. Moreover, a diabetic should be able among his friends to exchange his sugar ration for a fat ration.

As soon as diabetics are known in the country as a class demanding special privileges, just so soon I fear there will be added discrimination against giving them jobs or insurance. Already industrialists fear to employ diabetics because of their susceptibility to accidents and the increased hazard of an accident to a diabetic compared with a non-diabetic. If, in addition to this, the diabetics are to be known as a distinctive class and, in a way, pensioners on the rest of the country, it would be most unfortunate, but not so serious in the long run as for diabetics to perjure themselves by concealing their diabetes when interrogated. I know I demand a good deal of a diabetic, but I have always felt and said that diabetics as a whole were superior people, and I believe this is the time for them to prove it.

The diabetic is responsible for his immediate family aside from himself, and even his more distant relatives and his friends. He is aware of the dangers of obesity. He knows the necessity and advantage of the detection of diabetes at the earliest possible moment, and it is up to him to protect those about him.

March 30, 1920, there came to my office a woman with diabetes. She was given the usual examination with suggestions for treatment, and as it was impractieable for her to enter the hospital she was taught on the spot to examine her urine. She went home and shortly after contracted pneumonia and died. But in the intervening days amid her household cares she found time and took enough interest to examine the urine of 10 others in her boarding-house, and in so doing discovered the presence of diabetes in a boy. She gave him sound advice and sent him to his own physician, who also subsequently died, and later the boy came to me with this story. On the day she learned the Benedict test and made these ten urinary examinations for her friends, Louisa Drumm was aged seventy-nine years and four months. Can one not appropriately say to younger diabetic patients, "Go thou and do likewise"?

ALLERGIC PROBLEMS

By Gordon Chown, M.D.

Winnipeg

ALLERGY, with its multiple manifestations, is a complex subject, but through research we have arrived at a working basis from which the results achieved are comparable to those in any other branch of medicine. The practice of medicine, including surgery, is not an exact science, and this also applies to allergic diagnosis.

The diagnosis of the allergic condition is made perhaps more from a careful and complete history than from the other supplemental aids to diagnosis at our disposal. The taking of the allergic history, as suggested by Bray,[1] may be divided into predisposing factors, related to the onset of symptoms, and precipitating factors, specific and non-specific, which are related to the production of an attack.

A. *Predisposing factors* (related to onset): (1) Heredity: allergic predisposition has a strong tendency to occur in families. In infants and children, if careful inquiry is made an allergic family history will be obtained in over 60% of cases, which is more than 10% above the general average for all ages. Allergic children, especially if very young, are also more likely to have a bilateral positive history of allergy. (2) Tissue trauma; severe illness before onset of symptoms; *viz.*, (*a*) pneumonia; (*b*) infectious disease, *e.g.*, pertussis, rubella.

B. *Precipitating factors* (related to production): *Specific*, absorbed by: (1) inhalation: animals, hairs, feathers, dusts, pollens, moulds, fungi; (2) ingestion: foods, drugs; (3) injection: sera, drugs, bites, stings; (4) infection: bacterial allergy and worms; (5) contact: fabrics, chemical and physical agents. These are carried by the blood to the shock organ, with resultant allergic reaction. *Non-specific* (catalyzing factors): (1) dietary; (2) environmental; (3) toxic; (4) nasal; (5) psychic; (6) endocrine; (7) physical; (8) chemical; (9) mechanical. These lower the "allergic threshold" so that specific substances may act.

With this introduction I will limit myself to a discussion of only two phases of the subject, *viz.*, allergic rhinitis (vasomotor rhinitis); and bronchial asthma.

Allergic rhinitis.—In a review of recent literature, I was surprised to find three articles entitled "Sinusitis in Children", by otolaryngologists, Crooks,[2] London, 1938; Birdsall,[3] London, 1939, Gewanter,[4] New York, 1940; reporting a percentage of cures in children by local therapy and the Proetz displacement treatment. All articles mention that their results would not have been achieved without the complete cooperation of the pædiatrician with respect to regulating the routine of life and diet to include all the necessary vitamins. No mention, other than casual, is made of allergy being a possible causative factor.

Hansel and Chang[5] state that the otolaryngologist, the pædiatrician, and the general practitioner are frequently confronted with the problem of diagnosis and treatment in cases of recurrent colds, sinusitis, bronchitis, and recurrent pneumonia in children. These conditions are generally considered as infections, and the treatment usually consists of the administration of vaccines against colds, drainage of sinuses, or the removal of tonsils and adenoids. That these symptoms and signs may be allergic instead of infectious in origin has been emphasized by Piness and Miller,[6] Cohen and Rudolph[7] and Hansel and Chang. The allergic nature of these complaints is often not recognized until frank bronchial asthma develops.

I am in entire agreement with the statement of symptoms as outlined by Barnett,[8] a pædiatrician of Spokane: "With the commonly observed type of allergic rhinitis in children the parents complain that the child 'has one cold in the nose after another'." It is their observation that the cold lasts not for a few days only, but even for weeks. Also, after but a few days of relief, and for no apparent reason, the cold may suddenly recur. Even in the intervals between colds, the nose is stuffy, especially in the morning.

Sneezing, sniffling and nasal itching, obstruction, and discharge are characteristic. Epistaxis occurs frequently. The eyes may be red and itching; the speech is often nasal. Fever is not observed unless secondary infection complicates the allergy, but great irritability is usually observed in conjunction with these manifestations.

Difficulty in nasal breathing or lack of it tires the child and results in broken sleep. Insomnia

* Read at the Seventy-third Annual Meeting of the Canadian Medical Association, Jasper Park, Alberta, June 18, 1942.

may be aggravated by overdosage of ephedrine. The resulting fatigue is often a pronounced symptom but it is insufficient to require rest in bed. Too often the children are needlessly confined to bed for relief of their afebrile, non-infectious "colds" or for protection of their associates. Other members of the family, playmates or schoolmates do not become secondarily affected. In bed or confined indoors, the allergic child may be exposed to an aggravated atmosphere of the very inhalants to which he is sensitive.

If tonsillectomy and adenoidectomy have been performed for relief of such "colds" the parents often emphatically state that not only has relief not been obtained, but the "colds" are even intensified. Mouth breathing is frequently so manifest that the parents are persuaded the adenoids have recurred.

The gross changes in the nose are the result of œdema and eosinophilic infiltration of the tissues. The nasal mucous membrane is characteristically pale and œdematous. The secretion is usually serous or mucoid. Polyps may be associated with the condition but often disappear after control of the allergic factor. The membrane does not usually become red and thickened, and the secretion does not become purulent unless secondary infection develops. Œdematous or cystic changes in the paranasal sinuses may be associated with the condition.

The properly stained nasal secretion shows many eosinophils. In contrast, a predominance of neutrophils indicates an associated infection, which at times may be so severe that eosinophils are not found until it is disappearing.

In the child with a definite seasonal incidence of rhinitis, with the symptoms of sneezing, itchy pharynx, nose and ears, accompanied by lacrimation, the diagnosis is hay fever or pollinosis.

Asthma.—In Bray's study of 4,317 cases of asthma, where age incidence has been noted by decades, the percentage incidence of the combined findings are as follows.

First decade, 33.7%; second, 14.1%; third, 17.5%; fourth, 16.3%; fifth, 10.5%; sixth, 5.7%; later, 2.2%.

Amongst 1,390 cases arising during the first decade the percentage incidence per year works out as follows: First year, 22.25%; second, 17%; third, 13.5%; fourth, 10.75%; fifth, 10.25%; sixth, 8.5%; seventh, 6.25%; tenth, 1.75%.

From these figures it will be realized that one-third of all cases of asthma have their onset during the first decade, and in one out of every four such sufferers the onset will date from the first year.

In my experience asthma is rarely diagnosed in the first year, even in the first five years of life. The usual diagnosis is bronchitis. While I agree with Chevalier Jackson that "all that wheezes is not asthma", a careful history will exclude aspiration of a foreign body, more especially if there is a family history of allergy. In the infant or child no matter what the age, with audible wheezing, retraction of the chest with expiratory wheeze on auscultation, associated at the onset by a non-productive cough, and terminating on the third or fourth day with a productive cough or vomiting, with resultant expelling of mucus, temperature rarely above 101°, the diagnosis is asthmatic bronchitis. In simple croup or laryngeal diphtheria, the inspiratory stridor in contrast with audible wheezing is marked. Auscultation of the chest is negative. In laryngotracheal bronchitis, the child at the onset is extremely toxic, with a high temperature and within a short time presents the picture of a very acutely ill child.

Therapeutically, the diagnosis can be confirmed by the hypodermic administration of three to four minims of adrenalin. If relief from most distressing breathing is obtained within a few minutes, there can be only one diagnosis. Ephedrine hydrochloride by mouth is not as efficient for diagnostic purposes.

In order to evaluate my results, the following questionnaire was sent out to my private patients and to the public patients attending the Allergic Clinic at the Children's Hospital.

Do you consider the scratch tests and, as a result, the subsequent elimination of the food from the diet, or the substances from environment, *e.g.*, pets, feathers, dust, etc., were of value in effecting a cure, or in lessening the number of attacks of asthma or other allergic symptoms; *i.e.*, constant stuffed or running nose, associated with or without chronic cough? Answer Yes or No.

1. Elimination of a particular food or foods where applicable.
2. Elimination of pets, feathers.
3. Making a dust-free room.
4. Desensitization by needle.
5. Had the tonsils and adenoids been removed? With benefit? or without benefit?
6. Did your child have eczema as an infant?

In addition, your observations, critical or otherwise, of the treatment will be appreciated as a postscript.

PRIVATE CASES

41 questionnaires: 28 replied.

	With benefit	*Without benefit*
17 eliminated foods	12	5
25 eliminated pets, feathers	18	7
12 dust-free room	7	5
17 hyposensitized	17	0
12 tonsils and adenoids removed	6	6

15 of the cases had infantile eczema.

ALLERGY CLINIC, CHILDREN'S HOSPITAL

24 questionnaires: 15 replied.

	With benefit	*Without benefit*
15 eliminated foods	10	5
15 eliminated pets, feathers	9	6
15 dust-free room	8	7
15 hyposensitized	14	1
10 tonsils and adenoids removed	3	7

8 of the cases had infantile eczema.

In the majority of cases a child with eczema later developed allergic rhinitis or asthmatic bronchitis.

Elimination of food, pets and feathers, to which the patients were found sensitive showed an improvement in the majority of cases. Dust-free rooms, although rather difficult to cope with, proved advantageous in over half the cases where such treatment was tried. Removal of tonsils and adenoids does not solve the problem; patients were in most cases little if at all improved by removal.

In private practice, of the 28 heard from, 17 were hyposensitized. All of these, without exception have shown great improvement, gain in weight, and are now able to lead a normal life. Hyposensitization appears to be the most helpful method, when out of a total of 15 hyposensitized in the Children's Hospital Clinic, only one derived no benefit. These results were achieved in spite of unsatisfactory home environment, together with inability to co-operate to the fullest extent.

Farmer and Kaufman,[9] have recently reported their results in cases of perennial and seasonal rhinitis by hyposensitization with histamine phosphate (U.S.P.). The benefit obtained in perennial rhinitis compares favourably with desensitization to specific allergens, but not so favourably in seasonal rhinitis. With these encouraging results, it is possible in the near future that the treatment of allergic manifestations, including physical allergy, may be reduced to one common denominator.

Early in the paper it was noted that 60% of infants with allergic manifestations have a family history of allergy. No case history of an infant is complete without careful inquiry as to allergy, not only in the immediate family, but in the family tree. With a positive family history, certain preventive measures may be introduced with the hope that the infant will not become sensitive to the known foods and inhalants with high allergenic properties.

If the infant is breast-fed, breast feeding should be continued with the elimination of eggs from the mother's diet. If artificially fed, evaporated milk is indicated. Cereals, other than wheat or pablum, should be added to the diet first, namely, oatmeal, cornmeal, rice or barley. Vegetables should be added singly to the diet, rather than mixed vegetables or vegetable soups. Egg rates very high as a factor in producing asthma, allergic rhinitis, and other skin manifestations, and should be introduced gradually, and in my opinion not before eight months.

With reference to inhalants, feather pillows, eiderdowns, teddy bears or woollen toys, should be prohibited from the infant's crib and room. Pets, dogs, cats and canaries likewise, should be excluded from the surroundings.

As a dietary supplement, one of the concentrates is preferable to cod liver oil. In the occasional case, cevitamic acid tablets may be substituted for orange juice.

Linen or cotton-mesh shirts are recommended, to replace the ordinary woollen shirt.

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The most violent passions will sometimes allow us a respite, but vanity leaves us no repose.

—La Rochefoucauld.

Let Reason guide you at all times, even in the most unimportant things.—Pythagoras.

THE MANAGEMENT OF VESICAL NECK OBSTRUCTION*

By N. E. Berry

Queen's University, Kingston, Ont.

THE discussion of this question is by no means an innovation at urological meetings and this presentation in its final analysis concerns the operation of resection. This procedure is, I believe, now fully established, but I wish to present our experience and the methods which have greatly lowered our death rate in our clinic.

At this meeting two years ago an analysis was presented of operative deaths in patients over 70 in a large Canadian hospital. In carcinoma of the prostate it was 16% and in benign hypertrophy 13%, this latter figure being further subdivided into "punch" operation 7.7%, prostatectomy 24% and cystotomy 50%. I believe this is a fair, average picture, one that is absolutely unjustified and is a testimony to the very bad work that obtains generally throughout the country in these cases. Further, I might add that the high mortality rate, prolonged hospitalization, and unpleasant experiences of older methods of treatment of this disease are not altogether unknown to the public and deter many from seeking advice at the proper time. If better methods are available, it is our duty to tell the profession and the public. We are convinced resection is the answer; it is the procedure we ourselves would wish; it is the procedure that the doctors of our community demand for their patients and themselves.

I try not to be so dogmatic with our students about the question of which operation to perform; they will decide for themselves later, but I do try to keep them away from certain pitfalls in handling patients that were not stressed formerly, especially the notion that clear urine in a prostatic is a favourable sign. I teach them that it is better not to catheterize patients at all whom they believe to be carrying much residual unless there is complete retention or unless the man is willing to go to hospital. Regardless of how it is done, acute retention, cystitis and pyelitis may follow, and the doctor gets the blame. I do not think students were warned enough of this; they were told only that to empty an overdistended bladder completely was dangerous. That is true, but the risk is incidental to the patient's abnormal condition and is not greatly altered by the manner in which the bladder is emptied.

Original examination of patient.—When the patient is admitted he is given the same routine examination that it is customary to give to all genito-urinary cases. A rectal examination is made and a catheter passed to estimate the length of the posterior urethra, the presence of obstruction and the amount of residual urine. This catheter is usually tied in, and in most cases no further investigation is necessary. Cystoscopy is reserved for cases in which the residual urine is smaller than anticipated, in which there is undue bleeding, irritability of the bladder, or very dirty urine. In all cases of large unexplained residual urine, a cystogram and examination of cerebrospinal fluid is done. While there is not the same fear of operation as formerly, I think it is very well worth while to spend some time talking with the patient at the initial interview. By this, one not only forms an idea as to his bladder condition but also his cardiovascular system and kidney function, and his temperament, the amount of exertion he can stand, his appetite, whether he sleeps well, and whether or not his tongue gets dry. This information greatly assists in the accurate evaluation of the clinical situation and personal element. No amount of physical and laboratory examination is an adequate substitute. In cases which require treatment of the cardiovascular system, where renal function is seriously impaired or there is fever, preliminary drainage is employed, but we agree entirely with Creevy when he says that the patient in good condition, afebrile, and whose renal function is normal has nothing to gain and everything to lose from preliminary drainage.

In patients with large stones or very poor risks or those who will not tolerate urethral drainage a cystostomy is done. In three cases in our series this was done for calculi. In one patient who came in with profuse bleeding, spasms and a very large prostate this was done, but the symptoms continued with increasing fever, he developed septicæmia and died despite sulfonamides. This was our only operative death in the year, but cannot be charged to resection.

We recognize the following types of vesical neck obstruction: (1) fibrous prostate and contracted vesical neck; (2) middle lobe; (3) intravesical and intra-urethral; (4) sub-vesical; (5)

* Presented at the meeting of the Canadian Medical Association, Jasper Park, June 19, 1942.

carcinoma. I do not think that there is anyone who does not agree that the first two groups should always be resected and while they usually present the easiest technical problem there is much truth in Willinsky's statement that they may be the most dangerous. The allowable margin of error is less, there may be prostatitis, and disasters may occur. His statement that, "in the big prostate you can do no harm" has much to commend it. I would say that "you can do no harm resecting the big prostate if suprapubic drainage has been established", and recommend the beginner to follow this course rather than to start on the fibrous prostate. It is a much more innocuous procedure.

Some excellent articles have appeared by Dillon on the contracted vesical neck in younger people and by Fowler, who points out that

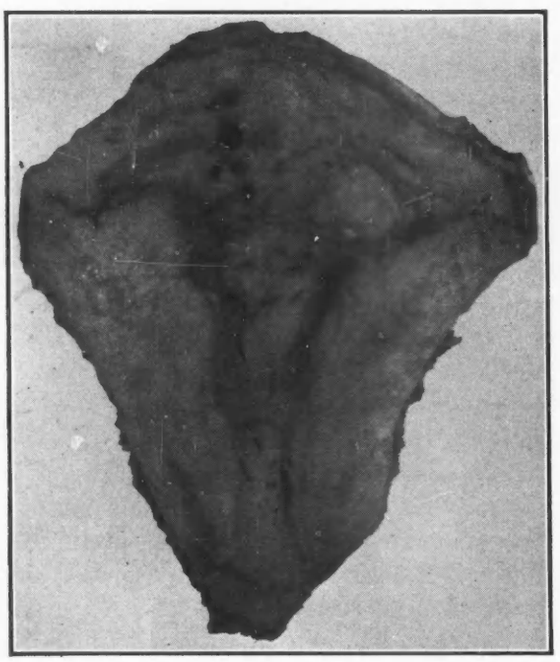

Fig. 1.—Carcinoma of the prostate showing the vesical neck following resection in 1939. Note extensive infiltration of bladder wall, but excellent vesical neck.

actual hyperplasia can occur in these younger patients. These cases are not common; none were met with in this series, but their occurrence should not be overlooked.

Carcinomata with obstruction should also be treated only by resection. I do not believe that permanent cystostomy is ever necessary and is a great injustice to any man. It is always possible to relieve retention and often satisfactorily and with good control, despite infiltrations of the urethra. This picture is presented of a patient who was resected in 1937 and 1939 and finally died of uræmia. It is by no means an isolated case (Fig. 1). The favourable influence of orchidectomy on prostatic carcinoma may obviate the necessity for resection in many cases. I have not yet practised it as a relief in obstruction, but my experience leads me to concur in the reported beneficial results.

It is in the larger types of subvesical and intraurethral enlargement that controversy as to the best method of operation exists. After an experience of 12 years, some years resecting more, other years enucleating more, I have been driven to the conclusion that all prostates can and should be resected and that the decision depends not on the size of the prostate, but the skill of the operator. I admit this is a broad statement and I know there are other viewpoints, but this conclusion has been arrived at only after the passing of years and the accumulation of the experience of more than seven hundred operations. Proficiency in resecting larger prostates is simply a question of experience. To some extent this has been the result of popular demand, but it has been accomplished without an increased mortality and the end has more than justified the means.

Until recently, all very large prostates had preliminary suprapubic drainage. This decreases the shock of the operation and complications, and simplifies the after care. I used to feel that, having opened the bladder, you might as well do a complete prostatectomy. I have changed my mind because you can proceed sooner with a resection than with prostatectomy; shock is less; there is no infected wound to open, and recovery is much more rapid. I think most of us with reliable memories will recall that some of these colossal prostates with subtrigonal extensions were difficult to enucleate and the postoperative course was eventful. They are also difficult to adequately resect, and indeed impossible, without the assistance of the rectal finger, but the experienced operator can assure a result in every way comparable to that obtained by prostatectomy.

Preparation for operation.—In my opinion to waken a patient at 6 a.m. give him an enema, no breakfast and morphine is the best possible way to invite nausea. We give an enema and barbiturate the night before, discuss the operation and allay the patient's fears. At 8 a.m. he is given fruit juice, coffee and toast, and usually no sedative. Most of my patients, like myself, are farmers and are poor and through-

out the operation we discuss matters of common interest. This helps both of us. Milner rightly states the patient is anxious to have his operation and relief, and sedatives are not necessary.

Anæsthesia. — We employ spinal anæsthesia exclusively. It has definite disadvantages and is by no means innocuous, but it is superior to anything else. For a long time we used procain only, in doses of 50 to 70 mgm. and found it satisfactory, but we have gradually changed to pontocain. Procain provided sufficient anæsthesia, but the prolonged effect of pontocain during the hours following operation lessens the amount of morphine required, adds to the patient's comfort, and lessens shock. The practice of combining novocain or 10% glucose with pontocain does hasten the anæsthesia, but we have not found it necessary: 10 to 12 mgm. of pontocain is usually satisfactory. We do not aim at having too profound anæsthesia as very marked relaxation is undesirable. The patient's head is slightly elevated at first. The table may then be tipped in any desired position that the operation or the patient's condition may demand. Fall in blood pressure is the most troublesome feature of this type of anæsthesia and occurs with sufficient frequency to detract from the method. I am not sure what drug, if any, will entirely prevent it. We give nothing routinely, but watch the pressure closely, and if there is an appreciable fall give ephedrine, coramine or neosynephrine. Postoperative headache is no consideration when the patient has to remain a few days in bed.

Operation.—As to the operation itself, I do not know that I have anything new to offer. We use the standard McCarthy instrument and a combination spark gap, valve tube machine, to energize the loop. We have only a standard obturator and find that with care there is little difficulty in introducing the instrument. It is my practice to begin the operation on the floor and then proceed to either side beginning at the vesical neck and, if necessary, withdraw the instrument so that the cut may be made to traverse the full length of the elongated urethra. This can only be accurately determined with the finger in the rectum and it is kept here at least half the time the operation is going on. I could not do the operation without the assistance of my own finger in the rectum. I am aware that some experts prefer to start anteriorly, claiming definite advantages in such a procedure. I have not tried this. It is my objective to push the prostate into the field and take everything I can engage in the loop. As succeeding portions are taken you can feel the prostate disappear from the rectal finger and actual prostatectomy is accomplished. This is not always necessary as many of our earlier cases were relieved by very incomplete operations, but to ensure a complete, satisfactory and permanent result it is advisable to remove most of the gland, and I think it has been a common experience that a complete operation carries no greater risk than an incomplete one. There are very large sub-vesical types in which the gland does not fall in readily and at the completion of operation there still appears to be a large prostate on rectal examination. I extend my resection along the floor of the elongated urethra, using my finger as well as the verumontanum as a guide to determine the position of the sphincter. There should be no question of injuring it.

Any very obvious vessels are coagulated as the operation proceeds, but no determined attempt is made to control bleeding until the completion of the operation. In some cases, most commonly sclerotic individuals, bleeding may be difficult to control, and even after considerable effort may persist. In such cases or in cases whose blood pressure may be low at the completion of operation additional vigilance is necessary.

Postoperative care.—For drainage we employ a No. 22 or 24 double eye soft rubber catheter of good elasticity and preferably a coudé tip. We have not found hæmostatic catheters of any real help and have discontinued their use. The necessity of constant attention, especially in the first few hours after operation, is so important that too much stress cannot be placed upon it. This work cannot be done without a competent staff. If clot is allowed to collect in the bladder after operation, bleeding may be difficult to control, the patient suffers unduly and serious complications are invited. Small pieces of tissue left in at operation may greatly add to the difficulty of proper irrigation and must be evacuated. When, through neglect or persistent bleeding, clot collects in the bladder, prompt decisions must be made as almost every case can be successfully handled if sound judgment is used. This clot must be evacuated without delay. I usually return the patient to the operating room and clean off all clot in an effort to locate bleeding points, sometimes having

trouble in accomplishing this. The only hæmostatics we use are morphine and transfusion. We feel it is most important to employ transfusion and believe it should be done before the patient becomes pale and sweating. In our series we did it five times, but should probably have done it oftener. The use of apparatus employed in our Red Cross Clinics greatly simplifies the taking of blood and I commend it to your use. One case is worthy of special note.

A patient discharged on the 6th postoperative day began to bleed the following morning; this persisted during the day, but he was able to void until noon, when clots began to cause difficulty. I did not see him till 7 p.m. when his bladder was greatly distended and I removed much clot. In spite of this profuse bleeding continued and I was forced to transfuse him, open the bladder, and pack the vesical neck. I doubt that this would have been necessary had treatment been possible sooner.

There is no doubt that the practice of certain clinics in keeping patients around for three weeks under observation is particularly sound, as it is during this period that hæmorrhage as well as other complications occur. I regret that most of our patients are so well long before that, that we cannot keep them.

Occasionally a stricture is seen at the meatus, but the most dangerous point is the peno-scrotal angle. If the instrument grips tightly here, great care must be exercised or a periurethral infiltration or actual abscess may ensue with resulting stricture. There have been two such cases in this series. This could be avoided by slow dilatation or introducing the instrument through a perineal urethrotomy. It is probably true that, in general, complications are less common after resection than prostatectomy, but are apt to be more severe when they do occur and call for prompt decisions.

The patient is allowed up on the 2nd or 3rd day and the catheter removed on the 3rd day unless the temperature is over 100°. If he does not void freely, further resection should be done within a few days, but today this is seldom necessary. If the bladder empties properly, the urine will clear up quickly, though I have had a couple of cases which were very slow for no obvious reason, but in two others there had been extensive resections and the patients had been in bed longer than usual. In these latter cases one should not hesitate to go back and clean off all slough and incrustations. I have not seen an ulcerating cystitis such as occasionally followed prostatectomy. In these cases the use of tidal drainage with an organic acid has been reported upon favourably.

Secondary hæmorrhage, sufficiently severe to require evacuation of clot, was met with in 4 cases. The first occurred on the 11th postoperative day. The patient was a diabetic. After the clot was cleaned out he had no further trouble and was discharged in 24 hours. The second was met with on the 9th day; he was an extremely bad case, carried a blood pressure —systolic 250, diastolic 150 and had a recent coronary thrombosis. He bled severely and was moderately shocked, but recovered promptly. The third had recurring hæmorrhages on the fifth and ninth days, sufficiently severe to require transfusion. The fourth has been reported above. One patient, while at work, on the twenty-eighth day passed a large clot with much bloody urine, but had no trouble before or since.

I do not think incontinence need ever occur from damage to the sphincter. I agree with Milner that it may result from incomplete resection. I have only seen it in one case of carcinoma in the early days of resection. I am surprised that it is not seen in some of these cases with extensive infiltration of the urethra.

SUMMARY OF 120 CASES

There was nothing unusual about the age group. There were no cases under 50. There were 10 cases between 80 and 85, 3 cases between 85 and 90 and 1 case between 100 and 200. This man was 3 months over the century mark and also had pernicious anæmia. I had a letter from his doctor only recently saying the old man had just died a "physiological death" 9 months after operation, but voided well to the end. There were several cases of known coronary thrombosis, extreme hypertension, cerebral vascular accidents and congestive circulatory failure. Three cases had preliminary suprapubic cystotomy for stone; 4 cases were complicated by carcinoma of the bladder and in 14 the prostate was carcinomatous.

We did not have an operative death during 1941 in our clinic in Kingston. In order to have mortality figures I have therefore included in our series all cases from January 1941 to May 1942, making a total of 120 cases with 3 deaths, an operative mortality of 2.5%. The first two occurred in succession; both were over 80 and really died of shock. The first was an advanced carcinoma and was probably inoperable. The third death was also from a car-

cinoma and the patient died of uræmia for no obvious reason. The group included both public and private cases and excluded four which were considered inoperable, but there were at least half a dozen patients operated upon who, in spite of their recovery, were also inoperable.

I think it is fair to say that the average saving in hospitalization over prostatectomy was 25 days, and in our public service someone has been saved at least one hundred dollars on every case. The private case is saved correspondingly more. In an appreciable number of these cases there is also a real saving in the time away from work. These economic considerations would not be justified if it entailed an increased risk for the patient, but with a decreased risk it would seem to make the argument decisive.

CONCLUSIONS

1. An experience of more than 700 resections with a summary of the last 120 is presented.
2. The death rate for the last group was 2.5%. There were 100 consecutive cases without a death.
3. All types of vesical neck obstruction can be dealt with by resection.
4. Results are in every way comparable to those achieved by any other operation.

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RETROPERITONEAL TUMOURS IN CHILDREN*

By Frederick Pilcher, M.D.

Calgary Associate Clinic, Calgary

RETROPERITONEAL tumours are of interest chiefly to pædiatrician, radiologist and urologist. These tumours are of especial interest to the urologist because a large proportion of them occur in the kidney and the others by their close relationship to the urinary tract may cause urinary complications either by pressure upon or by invasion of the ureter and kidney. Therefore, a urological examination becomes necessary in the diagnosis of a majority of retroperitoneal tumours.

Attention is called to the title of this paper "Retroperitoneal Tumours in Children". In the abdominal area of children, including the retroperitoneum, the vast majority of tumours are either embryomas (Wilms' tumour) of the kidney or neuroblastomas of the adrenal and retroperitoneal nerve tissue. Other retroperitoneal tumours in children are so rare as to justify little more than bare mention. In adults, on the other hand, a whole host of tumours would have to be considered in more detail.

Retroperitoneal tumours may originate from almost any of the various tissues in the space posterior to the peritoneum.[14] This includes fat, fascia, muscle, connective tissue, blood and lymphatic vessels, lymph glands, embryological structures, and portions of the autonomic nervous system. Of course, tumours of the pancreas, adrenal, kidney and ureter are also retroperitoneal. Some years ago all of these tumours were called sarcoma, and no definite effort was made to identify them. In more recent years, however, the exact nature of many of these tumours has been determined and they have been classified accurately. On account of the tremendous variation in the nature of retroperitoneal tumours, as well as the uncertain character of a number of them it is difficult to give a satisfactory classification. Table I groups retroperitoneal tissues, the kidneys and the adrenals. Table II gives a list of other types of abdominal tumours which have to be considered in a differential diagnosis.

TABLE I.

RETROPERITONEAL TUMOURS OF CHILDREN

A. Retroperitoneal Space Tumours
   - Benign — lipoma, fibroma, myxoma, angioma, dermoid, adenoma.
   - Malignant — sarcoma, fibrosarcoma, liposarcoma, teratoma, lymphosarcoma, *neuroblastoma*, lymphoblastoma (Hodgkin's).

B. Kidney Tumours
   - Benign—adenoma, fibroma, lipoma, cyst, etc.
   - Malignant—*embryoma (Wilms')*, hypernephroma, epithelioma of pelvis.

C. Adrenal Tumours
   - Cortex—adenoma, fibroma, carcinoma.
   - Medulla—ganglioneuroma, paraganglioma, *neuroblastoma.*

D. Retroperitoneal Metastases (testis, etc.)

In the retroperitoneal space, either near the kidney or in the cellular spaces more distantly removed, benign tumours may occur and have been reported but are extremely rare in children. These include myxoma, lipoma, fibroma, angi-

* Presented before the Section of Urology at the Seventy-third Annual Meeting of the Canadian Medical Association, Jasper Park, June 17, 1942.

oma and dermoid. Adenoma and cysts may originate from the Wolffian duct or other embryological remnants.

Malignant perirenal and retroperitoneal tumours[1] such as teratoma, fibrosarcoma and liposarcoma are extremely rare in children. Somewhat less uncommon than the above, but still very rare, is lymphosarcoma.[12] This malignant tumour occurs at an average age of about 45 years. A primary and prominent appearance retroperitoneally is rare at any age and very rare in children. Lymphosarcoma usually presents itself as cervical or intestinal lymphosarcoma. It may present a large mediastinal mass in children. The multinodal involvement and positive biopsy from an accessible gland usually give a correct diagnosis and prevent a needless abdominal exploration where abdominal masses are prominent. Retroperitoneal lymphosarcoma is the usual preoperative diagnosis for neuroblastoma either of the adrenal or of retroperitoneal nerve tissue. This second most common retroperitoneal or abdominal tumour of children will be discussed later. Lymphoblastoma (Hodgkin's disease) is less frequent than lymphosarcoma, especially as a prominent cause of retroperitoneal tumour. The associated enlarged spleen with positive biopsy from a superficial node usually leads to a correct diagnosis.

Embryoma, or Wilms' tumour, is by far the most common kidney tumour in childhood. Benign tumours of the kidney or its capsule such as adenoma, fibroma, lipoma and cyst are rare curiosities, usually accidentally discovered at postmortem. Hypernephroma has been described in childhood a few times. The symptoms are more likely to be similar to those in adults, with hæmaturia an outstanding feature. The exact diagnosis will probably be made only at operation. Wilms' tumour is the commonest retroperitoneal as well as abdominal tumour in childhood and will be described in detail after the other forms of retroperitoneal tumours have been mentioned briefly.

The adrenal gland being a retroperitoneal structure gives origin to tumours which must be discussed here. Lipoma, fibroma, angioma and cysts have been recorded. Adenoma of the adrenal is seldom large in size and gives rise to the genito-adrenal syndrome with precocious physical and sexual maturity. Carcinoma of the adrenal cortex is very rare and like adenoma may give rise to premature puberty with Addisonian pigmentation. Metastases occur early to the liver, lungs, kidney, or brain.

Among benign tumours of the adrenal medulla, ganglioneuroma occurs rarely, but almost exclusively, in children. Paraganglioma occurs rarely in children and only occasionally in adults. It may occur in other parts of the chromaffin system. Malignant tumour of the adrenal medulla or neuroblastoma is almost exclusively a disease of childhood. It is the second most common tumour of the abdomen in children. More will be said about it later. It is possible for retroperitoneal metastases such as occur from the testis to form a prominent tumour mass, but this seldom occurs.

Table II gives in brief outline the principal abdominal masses which must be considered in the differential diagnosis of retroperitoneal tumours. So far as diseases of the kidney itself are concerned, the majority of them can be recognized readily by intravenous or retrograde pyelography. The huge dilatation of calices and pelvis in hydronephrosis is readily seen. Polycystic disease is bilateral, which feature is of greatest importance in differentiating it from cysts and tumours. Solitary cyst of the kidney only rarely occurs in children and has its own characteristic features observed by pyelography. Perirenal hydronephrosis is a disease of obscure nature and difficult to diagnose. Only an occasional case has been observed in childhood.

TABLE II.

ABDOMINAL MASSES TO BE DIFFERENTIATED FROM RETROPERITONEAL TUMOURS

A. Diseases of kidney producing a mass
   - Hydronephrosis
   - Polycystic disease
   - Solitary cyst
   - Perirenal hydronephrosis

B. Intra-abdominal Masses
   - Neoplasm of liver
   - Enlargements of spleen (leukæmia, lymphoblastoma, etc.)
   - Tumours of ovary
   - Cysts of omentum and mesentery
   - Cysts of pancreas (actually retroperitoneal, but appear as abdominal mass)

Among the intra-abdominal masses to be ruled out in the differential diagnosis of retroperitoneal tumours, the most common, perhaps, is tumour of the liver. Enlargements of the spleen in leukæmia and lymphoblastoma have their associated alterations in blood counts and lymphadenopathy which make them fairly easy to recognize. Tumours of the ovary, cysts of the omentum, mesentery, and pancreas, have

their individual characteristics, which together with the information obtained by complete urological study should make them no special problems.

EMBRYOMA (WILMS' TUMOUR)

Embryoma of the kidney is a highly malignant tumour occurring almost exclusively in infancy and childhood.[6] It grows rapidly and usually silently. Metastases occur early and the outcome is usually fatal. These tumours have been classified in many different ways according to the predominating cell type, but have been most commonly known as Wilms' tumours.

CASE REPORT

A girl, five years old, was brought to the office on April 19, 1941, on account of gross hæmaturia and difficulty in the passage of clots from the bladder. Abdominal examination showed a mass in the upper left quadrant which extended about three inches below the costal margin and filled the upper abdominal quadrant to the midline medially. It could be palpated bimanually with the fingers in the costomuscular angle behind and a hand on the abdomen in front. General physical examination was essentially negative. The blood counts were within normal limits. An x-ray plate of the chest was negative. An intravenous urogram on April 22 demonstrated a normal kidney on the right. No dye appeared in any of the films on the left side. There was the shadow of a soft tissue mass filling the upper left abdominal quadrant. The following day cystoscopy was performed and a normal bladder disclosed. A retrograde pyelogram on the left side (Fig. 1) showed a distortion of the calyces compatible with tumour.

High voltage x-ray therapy was started two days later and continued for two and a half weeks, giving the maximum dosage which the skin would tolerate. About two and a half weeks after this therapy was completed the abdominal mass had shrunken until it could no longer be found on abdominal examination. Transperitoneal nephrectomy was performed on May 28. No metastases could be found anywhere in the abdominal cavity at the time of operation. Apparently the tumour had not invaded the surrounding tissue or the renal vein. The tumour and kidney were removed together with as much of the surrounding tissue as possible. A transfusion was given immediately following operation. Postoperative convalescence was relatively uneventful. About four weeks after the operation an appropriate course of deep x-ray treatment was again given.

The child appeared well until December, when she began to lose weight and did not feel well. At the time an x-ray plate of the chest showed several definite areas of secondary carcinoma. At this time an abdominal mass became palpable in the operative area. From then the course was progressively downward and she died February 21, 1942, ten months after the onset of symptoms. A postmortem examination was not done.

Etiology.—As with all other malignant tumours the cause of embryoma is unknown. However, it is probably of congenital origin. The mixed character of this tumour has led to almost every conceivable possibility being offered as an explanation for its origin. It hardly seems necessary to review all of the theories here. Geschickter and Widenhorn[5] are probably correct when they state: "Approximately two-thirds of all Wilms' tumours contain only those

Fig. 1.—Retrograde pyelogram showing deformity compatible with Wilms' tumour.

microscopic elements of spindle cells and early tubule formation which can be found in the normal embryonic kidney in normal infants a few months after birth. The majority of these tumours, therefore, are of normal developmental processes occurring in the growth zones of the renal cortex in late fetal life or in the first few months after birth. The occurrence of cartilage, bone or muscle in approximately one-third of these new growths is not strange when we consider that the more undifferentiated mesenchymal spindle cells found in the normal nephrogenic tissue in the process of development may retain the multiple potentialities for the elaboration of all the normal mesenchymal derivatives."

Pathology.—Wilms' tumour is usually unilateral although bilateral cases have been reported. A majority of the tumours are large and they may fill the abdominal cavity and weigh one-third as much as the patient. The tumour is usually well encapsulated and destroys the kidney by pressure. Its shape is usually round or oval, but it may be lobular. The mass is generally solid but may contain cystic, hæmorrhagic, or necrotic areas. The tumour may in-

vade the renal vein and metastasis probably occurs most frequently by this route, since secondary nodules are so commonly found in the lung and the brain. Extension may occur directly to the surrounding tissues or by way of the lymphatics to the adjacent lymph nodes. The microscopic picture varies greatly in different areas of the same tumour or when one tumour is compared with another. The predominance of one cell type over another has led to various classifications of the tumour. The character of the predominant cell type apparently has no bearing on the clinical course or the prognosis. There may be partially differentiated or undifferentiated epithelial and connective tissue cells showing various degrees of cellular activity in different parts of the same tumour. There are usually masses of poorly differentiated cells forming structures resembling embryonic uriniferous tubules or even abortive glomeruli. These are embedded usually in a heterogeneous supportive structure composed of undifferentiated round and spindle cells with the possible presence of smooth and striated muscle. Bone and cartilage may occur rarely.

Symptoms.—Wilms' tumour is chiefly one of infancy and early childhood, there being very few cases after the age of ten. Rare cases have been reported in adults even up to middle age. The average age is around two to three years and two-thirds of the cases occur before the age of three. There seems to be no significant difference in sex incidence. Either kidney is affected about equally often.

The most common first symptom is an abdominal mass discovered by the parent or nursemaid who accidentally sees or feels it. Symptoms referable to the urinary tract are conspicuously absent. Gross hæmaturia occurs in only 15% of the cases and is a bad prognostic sign. Pain, loss of weight, anæmia, and symptoms due to pressure on other organs such as vomiting, constipation, dyspnœa and œdema are late symptoms and evidence of far advanced disease. Often the child maintains an excellent state of health even with a large tumour.

Abdominal examination shows a mass filling one upper abdominal quadrant extending to the level of the umbilicus or even into the pelvis. It may extend beyond the midline toward the opposite side. The mass can be palpated bimanually with the fingers of one hand in the costomuscular angle and the other hand over the abdomen in front. This locates the tumour in the kidney position and helps considerably to differentiate it from other abdominal as well as other retroperitoneal tumours. The mass is usually smooth, movable and insensitive. The urine is generally normal.

A plain x-ray film of the abdomen is of value to rule out stone, but the soft tissue shadow of the tumour is not of any diagnostic value. The pyelogram obtained either by the intravenous or retrograde route is the most valuable aid in diagnosis. It will at once rule out hydronephrosis, pyonephrosis, and polycystic disease. The presence of a normal kidney on the other side is established, which is especially important before proceeding with operation. The pyelogram on the diseased side may show characteristic distortion or filling defect of tumour and displacement of the pelvis. An almost normal pyelogram is possible however. Retroperitoneal neuroblastoma is the most likely tumour to be confused with embryoma, especially since it may displace the pelvis as much as embryoma, and by infiltration of the kidney produce a similar pyelogram. In some cases only by operation and biopsy can the two be differentiated. However, in at least 90% of the reported cases there is a deformity compatible with tumour and this together with the location of the mass make the diagnosis fairly certain. Previous mention has been made of other retroperitoneal tumours and abdominal masses likely to cause confusion. An x-ray film of the chest should be made in search for lung metastases.

Treatment.—The most important part of the treatment is operation. The value of x-ray therapy and in what stage of the treatment it should be employed are debatable. It is generally agreed that nearly all Wilms' tumours are very radiosensitive, but no proved Wilms' tumour has been cured by radiotherapy alone. In every operative specimen examined following radiotherapy living tumour cells have been found. Until recently the majority of men have employed preoperative radiotherapy followed by nephrectomy at an appropriate interval, usually about two or three weeks, and then a postoperative course of high voltage therapy.

Ladd and White[8] question the value of preoperative radiotherapy on the following basis. The longer operation is delayed, the more opportunity there is for metastasis to occur. Irradiation first softens the tumour and later

shrinks it by scar and connective tissue replacement and contraction. It seems reasonable to assume that metastasis might occur more readily while this change is taking place. Further, in patients who have died of remote metastases no local recurrences have been discovered at post-mortem. If nephrectomy had been done before metastasis occurred the child's life would have been saved. No one knows when metastasis occurs. If nephrectomy had been performed a month or week or even day earlier the metastasis might not have occurred. Therefore the delay produced by giving preoperative radiotherapy might have permitted metastasis to occur.

In a review of the literature by Ladd and White of 503 cases, there were 26 cures in which it was stated definitely whether preoperative radiotherapy was used. Of these 26 only 8 had received preoperative roentgen treatment. In Ladd and White's own series of 14 probable cures only one had received preoperative treatment. On the basis of these statistics it is clear that the chance of survival is greater if immediate nephrectomy is performed rather than delaying operation until after x-ray therapy. The only argument in favour of radiotherapy, then, is that it generally reduces the size of the tumour, thereby facilitating the operation and reducing the operative mortality.

The operative risk can be minimized by transperitoneal nephrectomy and by better preoperative and postoperative treatment. All of the case reports in the literature suggest that in recent years the operative mortality has diminished considerably. The transperitoneal approach for kidney tumours, as recommended by Cabot,[2] has many advantages over the usual retroperitoneal approach by flank incision. Cabot's incision extends from the tip of the twelfth rib forward and obliquely downward, parallel to the course of the main nerve trunks to the midline. The rectus muscle is cut across. The incision then extends up the midline as far as is necessary to give proper exposure. Thus the nerve supply of the rectus and other muscles is not disturbed, and solid healing without weakness in the abdominal wall follows. Abdominal exploration can be carried out at this time in a search for metastases and likewise to establish the diagnosis with certainty. The colon is pushed toward the midline and the posterior peritoneum over the tumour incised. This gives ready access to the renal pedicle, which can be tied before mobilization of the tumour and kidney. In this way metastases that might occur from handling of the tumour are prevented and loss of blood is reduced to a minimum. Larger tumours can be removed successfully by this method than by the lumbar approach and there is less chance of assuming that the tumour is inoperable. Further, a more radical removal of adjacent lymph glands and perinephritic tissues is possible, increasing the probability of cure.

The value of postoperative radiotherapy is perhaps even more questionable than that of preoperative radiotherapy. Since this form of treatment has never yet been shown to cure a recurrence its use can be considered only as a prophylaxis against recurrence. However it does not have the disadvantage of preoperative radiotherapy in delaying the operation beyond a time at which cure might have been obtained.

The prognosis is not so unfavourable as was once thought. Priestley[10] reported four cures out of 37 cases and Kretschmer[6, 7] 3 out of 24. Ladd and White, on the other hand, report 14 cures out of 60 cases. Their higher survival rate suggests the decided advantage of early operation as advocated by them. The size of the tumour and the cell type seem to have no bearing on prognosis. Gross hæmaturia and invasion of the renal vein are bad signs. Practically all such patients die. The younger the patient, the greater the probability of cure. In Ladd and White's series half their patients in the first year of life were cured. If recurrence is going to occur it is likely to be apparent within four months. If no recurrence is demonstrable in nine months, cure is reasonably certain and almost no cases have had a recurrence appearing later than two years after the operation.

NEUROBLASTOMA

Neuroblastoma[9, 11, 13] is the malignant tumour of the retroperitoneal space which in the past has been commonly present when the preoperative diagnosis was lymphosarcoma. It is the second most frequently encountered abdominal tumour in childhood, occurring approximately half as often as Wilms' tumour. The primary tumour may arise in any of several locations. Although it arises most commonly in the adrenal medulla, it may arise also in paraganglionic tissue adjacent to the adrenal gland, the cœliac plexus, the organ of Zuckerkandl, the superior cervical ganglion, and in other sympathetic nerve tissue, both retropleural and retroperi-

toneal. Farber[4] does not think that continued use of such terms as "Hutchinson's type" and "Pepper's type" is justified in view of the present knowledge concerning these tumours. The character of the metastases determines the type, and the location of metastases is in turn determined by the differences in distribution of lymphatics of right and left adrenals.

When occurring retroperitoneally these tumours may form a large abdominal mass. There may be clearly definable metastases to the liver, orbit, skull, long bones and adjacent lymphatic glands. A severe anæmia and fever are usually associated.

To differentiate this tumour from Wilms' tumour preoperatively may be difficult or impossible. It may invade the kidney and produce a pyelogram and gross specimen indistinguishable from Wilms' tumour. On the other hand Wilms' tumour may grow outwardly from the kidney and leave a normal or almost normal pyelogram. The essential thing is to determine by urological study that a normal kidney exists on the other side in case it should be necessary to remove one kidney. The exact location and nature of the abdominal mass may be determined only at operation.

Whenever this type of tumour is suspected immediate operation is recommended by Farber and Ladd[8] with removal of the tumour, if technically possible. After this the question of postoperative radiotherapy can be decided. It may be valuable and successful, for even in the presence of metastases there have been some spectacular cures following operation and radiotherapy.

Summary and Conclusions

The largest proportion of abdominal tumours in children are Wilms' tumours of the kidney. Neuroblastoma is second in frequency of occurrence. Both of these are retroperitoneal tumours. Other retroperitoneal tumours in children are rare and other abdominal masses uncommon.

Any of the renal or extrarenal tumours may, by pressure upon or invasion of the ureter and kidney, cause urinary tract symptoms and complications.

It seems best to consider every solid abdominal mass in early life a malignant tumour until proved otherwise by pathological examination. After a short but thorough preliminary examination and preoperative preparation immediate operative removal is advisable. Delay is dangerous. The few weeks required for preoperative radiotherapy may be enough time to permit dissemination of tumour cells. Following an immediate operation, preferably transperitoneally, subsequent radiotherapy may be considered.

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MYASTHENIA GRAVIS*

By Richard D. McKenna, B.A., M.D.C.M.

Montreal

THE purpose of this discussion is to survey the present status of knowledge of myasthenia gravis, from a review of the literature and the cases which have been followed in this hospital.

The first description of myasthenia gravis was given by Willis in 1672 and the syndrome was more clearly delineated by Erb in 1878. In 1895 Jolly suggested that muscles were the site of the disease. Oppenheim in 1899, noted hyperplasia of the thymus and in 1900 Weigert described a thymic tumour in association with myasthenia gravis. Buzzard demonstrated lymphocytic infiltration in muscle in one case. Milestones in the management of the disease state are the accidental discovery of the efficacy of ephedrine by Edgeworth[4] in 1930 and the work of Walker[26] with prostigmine in 1935. The etiology of the disease remains obscure.

* Department of Medicine, McGill University Clinic, Royal Victoria Hospital.

Rothbart[16] described the occurrence of myasthenia gravis in four siblings. Viets[22] has seen no evidence of hereditary factors in the 85 cases which he has followed. No other suggestion of an hereditary influence is seen in reviewing the literature.

Infection is undoubtedly a precipitating and aggravating factor. Rosenow and Heilman report that they have isolated from the nasopharynx of patients with myasthenia gravis a streptococcus not present in other individuals. They claim to have produced a myasthenia-like syndrome in experimental animals by inoculation with this serologically type-specific organism. This work, however, has not been widely accepted as proof of infection playing a major rôle as the etiological agent.

Primary disease of the central nervous system and of muscle itself lacks histological evidence, except for the non-specific lymphorrhages seen in the muscles.

There have been numerous references in the literature to the relationship of the thyroid to myasthenia gravis. It may be stated that while its co-existence with hyperthyroidism is rare, muscular atrophy and generalized muscular weakness are frequently seen in thyrotoxicosis. Thorner[21] and also Cohen and King[3] have recorded cases of combined disease in which the symptoms of myasthenia gravis were at a minimum when the thyrotoxicosis was greatest, and as the thyrotoxicosis waned the myasthenia reappeared. Thorner feels that the two diseases are mutually antagonistic. Kowallis *et al.*[5] report four cases of combined disease and detail one case, which, following thyroidectomy, was relieved over a period of two years of symptoms of both myasthenia and hyperthyroidism. Plassman[13] believes that the thyroid and thymus are integrated through the parasympathetic system into a complex biological mechanism, so that changes in the one are reflected in the other.

Much has been written of the relationship of the thymus gland to myasthenia. Adler claimed to have produced a myasthenia-like syndrome in dogs by injection of thymus extracts. Other workers have, however, failed to confirm these findings. (The growth effects of thymus extracts, I believe, are now thought to be due to glutathione.) Thymic abnormalities are reported as being present in approximately 50% of the 110 autopsy cases recorded in the literature. This abnormality has been described as either tumour or hyperplasia. Bell in 1917 made a review of these and the list was added to by Norris and recently by Miller[11] at Johns Hopkins. Meggandorfer and Meister reported two cases of myasthenia gravis associated with metastasizing thymic growths. This co-existence is, however, a rarity.

Unfortunately, terminology in classification of the forms of thymic disease has been inexact and confusing. Norris considers the pathological changes in the thymus in myasthenia gravis as conditions of greater or less degree of epithelial hyperplasia, and that, when the hyperplasia is extreme, a localized and at times encapsulated tumour-like mass is formed. In instances of extreme hyperplasia lobulation is not in evidence; few lymphocytes and almost no Hassall's corpuscles are present in the epithelial mass. Ewing classifies tumours of the thymus as carcinomata, lymphosarcomata, and a mixed process similar to Hodgkin's granuloma.

Blalock in 1939 reviewed the literature of associated thymic abnormalities and myasthenia gravis and mentions three previous attempts to influence the course of the disease by thymectomy. Of these, two patients died in the postoperative stage and the third, while showing no gross or histological thymic abnormality, is described as being improved three years later. At that time he reported an operation of his own on a case of myasthenia gravis. The patient, a short time postoperatively, was subjectively improved. In this case, the pathologist was unable to find any histological evidence of thymic tissue in a cystic superior mediastinal mass, which had previously been subjected to deep x-ray therapy. In a recent article Blalock[1] reports six cases in which thymectomy was performed in treatment of myasthenia gravis. He states that all except one thymus showed hyperplasia and that improvement has occurred in three cases; no improvement has occurred in two cases; and one patient died in the postoperative phase.

Extensive studies have been made in blood and muscle chemistry during the past few years. It has been well established by many observers that the composition of potassium, phosphorus, glucose, urea, creatinine, amino acid and uric acid is not remarkable in myasthenia gravis. Reinhold and Kingsley,[15] in chemical analysis of muscle, found an ex-

ceptionally high concentration of soluble ester phosphorus. Nevin[12] reports that the phosphorus-holding compounds in myasthenic muscle are normal.

According to Cummings the affected muscles in persons suffering from myasthenia gravis contain more potassium than do normal muscles. He reports that after the subcutaneous injection of prostigmine the muscle potassium falls, but that there is no increased urinary output. The potassium appears to be retained in the blood and returns to the muscles as weakness in the muscles reappears.

Milhorat and Wolff[9] found that the creatine excretion of those afflicted with myasthenia gravis is only slightly greater than that of the control subject, except in severe relapses and in those in whom the disease was rapidly progressing towards a fatal termination. These persons often excrete large amounts of creatine and show a serious defect in their ability to retain ingested creatine. The authors feel that the fundamental metabolic disturbances in myasthenia gravis are not centred in the metabolism of creatine, but rather that the metabolism of creatine is involved secondarily. When the metabolic processes are seriously involved prognosis for life is grave. Contrary to Milhorat and Wolff,[9, 10] Meredith[8] reports a fall in creatine output with prostigmine therapy.

The prevailing theory as to the pathogenesis of the disease is that there is some interference with transmission of impulses across the myoneural junctions. It has been established that at the synapse, acetylcholine is secreted at the time of the passage of the impulse and that the amount of acetylcholine or the length of time that it is available is controlled by a destructive chemical substance, cholinesterase. It was at first postulated that interference in transmission of impulses was due to cholinesterase over-activity, resulting in the increased rate of hydrolysis of acetylcholine, but McGeorge[7] and also Russel[17] have shown that serum cholinesterase activity is not unusual and is of the same order as found in control subjects. In addition, Milhorat has shown that spontaneous changes in muscular debility in myasthenia gravis were not accompanied by changes in esterase activity. Again, whereas prostigmine depresses cholinesterase activity in all individuals, as shown by McGeorge, in patients with muscular debility resulting from other conditions than myasthenia gravis no therapeutic effects are seen. Two cases in which cholinesterase activity of muscles was determined are reported as showing normal values. While it may be that serum and muscle cholinesterase values do not represent the state of balance at the myoneural junction, positive evidence of a disturbance at this site is wanting.

From a clinical viewpoint, the disease is uncommon, but occurs with equal frequency in either sex, from infancy to old age, and without respect for race or climatic condition. The diagnosis rests on a history of and later demonstration of muscular fatigability, more often first involving eye muscles. Initial involvement of skeletal muscles does occur in some cases. It appears however, that in a large proportion of the cases weakness is noted either initially or later in some or many of the muscles supplied by the cranial nerves. Symptoms are characteristically improved by rest, hence less marked in the mornings, aggravated by muscular exertion and infections, particularly those upper respiratory in type. Aggravation of symptoms or exacerbation of symptoms is associated with menstruation, whereas the effect of pregnancy, labour and nursing is usually favourable (Viets[25]).

Differential diagnosis includes progressive muscular dystrophy, bulbar palsy, thyrotoxic myopathies, psychoneuroses and chronic fatigue states, intracerebral neoplasms and ophthalmoplegia from focal lesions. Neurological and cerebrospinal fluid examination is invariably negative. Myasthenia muscle reactions, namely loss of response to higher frequencies of faradic current, while not invariably demonstrable in myasthenia gravis, and present in thyrotoxic myopathies, are of definite diagnostic value. The therapeutic test of prostigmine as outlined by Viets and Schwab[24] is most useful and reliable; improvement in muscular weakness shown by ergogram, electromyogram or on fluoroscopic observation of the swallowing reflex (after the ingestion of barium paste), is considered to be pathognomonic of the disease.

Iodine favourably affects the muscular weakness of thyrotoxicosis but leaves myasthenia gravis weakness unaffected. Quinine causes temporary improvement in myotonia and aggravation of myasthenia gravis symptoms.

Of the multitude of drugs, hormones, and vitamins that have been tried in the management of the disease, thymic extracts, cortin, pituitary extracts, thiamine chloride and tochopherol have not been of proved value. Ephedrine[4, 14] and potassium salts[20] have both been found useful, either individually or in combination with prostigmine. Guanidine hydrochloride and glycine[2] are of value only in combination with prostigmine. Prostigmine bromide by mouth in 15 mgm. tablets appears to have been the mainstay of treatment in the hands of the majority of workers. Rarely is it necessary to administer the drug (prostigmine methylsulphate) by injection, and this form of therapy is reserved for patients with severe forms of respiratory embarrassment. Individual requirements vary greatly, but in Viets' experience the average maintenance dosage is six to eight tablets daily. Occasionally, especially in the initial use of the drug, atropine is of value in reducing the increased peristalsis resulting from prostigmine administration. The mechanism of action in myasthenia is not well understood, but both potassium and prostigmine are thought to exert their action through the myoneural junctions.

No particular complication occurs in myasthenia gravis, and death is usually the result of involvement of the muscles of respiration, most often precipitated by an upper respiratory infection.

Twenty-five per cent of the cases are reputed to have remissions, the average length of which is 2.2 years. The entire course of the disease varies considerably, ranging from acute cases with death in a month, through the subacute cases, in which death occurs in 12 to 20 months, to the cases which go over a period of 8 to 10 years, with remissions and exacerbations and, finally, death from involvement of respiratory muscles.

Survey of 110,000 admissions to this hospital reveals 21 cases of myasthenia gravis (an incidence of approximately one in 5,000 cases). Twelve of the cases were male and 9 were female.

The average age of onset of symptoms in this group was 33 years, with a range between 11 and 67 years.

Follow-up, for periods of 2 to 7 years, has been possible on 15 cases. According to McEachern[6] none has shown a complete remission at any time.

The eyes were involved first in 15 of the cases, either in the form of lid droop or diplopia. One case showed initial involvement of the muscles of respiration. Interference with the power of speech was noted first in 4 cases. Initial involvement of extremities occurred in 4 cases, and of this latter group the lower extremities were involved first in three out of four cases.

A patient with associated hyperthyroidism had a marked exacerbation of her myasthenia gravis symptoms eight days after thyroidectomy. In another, with definite but mild hyperthyroidism, it was felt that the symptoms were due predominantly to the myasthenia gravis and thyroidectomy was not performed. Two cases in the series were found to have basal metabolic rates of –21%. Clinically, however, neither of these cases was considered to have hypothyroidism although the curves were entirely satisfactory. Two cases were seen to have myasthenia, clearly not myasthenia gravis, in which mild diabetic states were shown to exist. Muscular fatigability was improved in these individuals on routine (diabetic) dietary management.

Five of our cases have come to autopsy and it may be stated, that there were no constant abnormal gross or histopathological lesions.

Two cases showed marked and atypical thymic hyperplasia and lymphorrhages in skeletal muscle. The thymus in a third case was persistent and, (in a 30-year old woman) weighed 15 grams. Histologically, it was preadolescent in type.

In this case and in two others in which the thymus was atrophic and considered normal for that age-group, no lymphorrhages were found in the skeletal muscles. One of those having marked and atypical thymic hyperplasia (8 x 7 cm.) showed foci of lymphoreticular hyperplasia in the thyroid similar to that met with in the thymus. Some thyroid hyperplasia was seen in one case in which the thymus was not enlarged.

SUMMARY

1. There is insufficient evidence of a causal relationship between the thymus gland and myasthenia gravis and hence thymectomy and irradiation do not appear to rest on a firm basis, but should be more fully explored.

2. The general character of the disease strongly suggests a metabolic disorder. The

neuromuscular fault is at the myoneural junction.

3. Management, while purely palliative, is satisfactory. A combination of ephedrine and prostigmine appears to be the most useful.

4. It is evident that, despite the fact that from a therapeutic point of view much can be done for the patient afflicted with myasthenia gravis, both to prolong life and make it compatible with a useful and tolerable existence, the basic etiological factor and the pathogenesis of the disease are not known.

(The following references are only a partial list. A much more complete bibliography has been prepared by the author, and may be had from him on request.)

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The practical field of treatment (of asthma) is full of controversial issues. The allergists measure everything in terms of protein sensitivity and miss the solution sometimes because of failure to take into account certain defects of metabolism. The therapeutic empiricists scorn protein tests and bank on one line of action —surgical or medical. Between these two bodies of workers swarm the quack curers and asthma medicine vendors—and the last state of the patient is often worse than the first.—D. P. Marais, Treatment of the Asthma Syndrome, Clinical Proceedings, Cape Town Post-Graduate Med. Ass., 1942, **1**: 167.

WHAT SIGNIFICANCE HAS UTERINE RETROVERSION?*

By Evan Shute, B.A., M.B., F.R.C.S.(C)

London, Ont.

HISTORICAL BACKGROUND OF THE THEORY THAT RETROVERSION IS SYMPTOMATIC

LILLIAN FARRAR[1] mentions that Kohlrausch in 1854 claimed that the position of the uterus depended only on the fullness of the bladder and rectum. In the same year also, Cruveilhier expressed the opinion that there was no established normal position of the non-pregnant uterus and Mathews Duncan expressed a somewhat similar view. In Koch's classic work of 1880 on the position of the uterus it was concluded that the uterus had no absolute, but only a relative, position.

Sir John Williams, who later delivered Edward VIII, seems to have been the first to conclude (in 1876) that there was any association between uterine retroversion and menstrual complaints. He ascribed dysmenorrhœa to a congestion, caused by the constriction of the corpus uteri and the veins in the broad ligaments by the sacro-uterine ligaments. This conclusion, which he reiterated in 1885,[2] he based on the study of a solitary post-mortem uterus which showed, when removed from the body, marks where these ligaments had constricted it although its retroflexion had been but slight.

Later writers ascribed both menorrhagia and leucorrhœa to uterine retroversion. Herman adopted the retroversion theory enthusiastically and embodied it in his textbook of 1907, although he admitted that symptomatic retroversion occurred in only one case in ten. Jellett in his textbook said that retroversion always caused endometritis — hence symptoms ensued "almost invariably". Bland-Sutton and Giles ascribed certain vague pelvic symptoms to simple retroversion, but said that pain, leucorrhœa and metrorrhagia followed when inflammation coincided with it. Blair-Bell ascribed menorrhagia to chronic retroversion. Fothergill also believed that retroversion was harmful. Eden, Lockyer and Whitehouse[3] were more skeptical and expressed the view that many cases in adults were congenital or fortuitous. But Ten Teachers[4] blame retroversion for

* Read before the Noonday Study Club of Western Ontario, at London, on November 4, 1942.

chronic congestion, chronic subinvolution, and cervical infection, and list many pelvic symptoms such as backache, menorrhagia and sterility as its sequelæ.

Prof. Archibald Donald[5] in 1924 reiterated the opinion that he and Shaw had previously published in 1910. He began: "I need not conceal from you at the outset that it is a subject on which I hold very strong views and that these are not the views of the majority of gynæcologists all over the world. But I believe that the general opinion is based on a false pathology, and that, apart from a few exceptional cases, these operations are unnecessary and in many cases distinctly harmful." He went on to quote Mathews Duncan in this connection: "The subject is surrounded in a mist, and I do not myself know the straight and scientific road . . ." But, Duncan continued: "a retroverted, a retroflected, or anteverted or anteflected, or a laterally displaced womb does not cause any pain or disorder or disability. Thousands of blooming, happy, fertile women have displacements."

Of the symptoms sometimes seen in association with retroversion Duncan had stressed backache, bladder trouble, rectal trouble, but did not mention menorrhagia or dysmenorrhœa. Donald strove to upset the old theory that the retroverted uterus was congested, and his excellent paper should be consulted for the evidence he adduced to support his opinions. He concluded: "Complications are generally the only things that matter in retroversion, and not the displacement itself—none of these complications are produced by retroversion." "In a certain number of cases", he admitted, "a backward displacement seems to cause local pelvic discomfort and aching in the lower abdomen." He continued: "There is no doubt that in some few cases benefit follows the insertion of a pessary, but I am convinced that in most it is merely a faith cure, or cure by suggestion; otherwise the relief obtained would often seem inexplicable." The pessary often gives relief, he pointed out, when it is too small to affect the uterus, or is improperly inserted, or has not corrected the retroversion at all, or is out! Mathews Duncan, too, noted this with amusement—as have all of us! Donald ascribed the benefit received to some effect of the pessary on the sympathetic nervous system. He admitted that retroversion was undoubtedly a factor in causing sterility and abortion. He inveighed against the poor results of suspension operations, their danger, the risk that they become such a routine as to blind the surgeon's judgment, and their power of suggestion. Yet he admitted that he had had to do four suspensions in the preceding four years for symptoms of retroversion not relievable in any other way.

Melhado[6] recently pointed out that in 25% of healthy women the uterus was retroverted. He went on: "In the matter of symptoms and signs, it may be fairly said that their presence is in no sense a characteristic of retroversion, or any other displacement, and so the displacement may be but a coincidence, and possess no etiologic factor whatever." He reviewed 261 retroversions seen in Montreal and could not conclude that retroversion *per se* accounted for any of their symptoms. He suggested that suspension operations might possibly assist retroversions associated with severe prolapse, but offered no other indication for the operation.

H. O. Smith[7] found 1,320 cases of retroversion among 5,412 women examined, an incidence of 24%.

RETROVERSION IN GYNÆCOLOGY

The complaints most commonly ascribed to uterine retroversion nowadays are sterility, menorrhagia, dysmenorrhœa and backache. I have reviewed my records for several years back and selected from them all cases having these and a few other such common gynæcological complaints. The results are tabulated below with respect to uterine position. It should be pointed out that all cases have been excluded from consideration where there was retroscession (mere retro-displacement of the uterus as a whole, without alteration in the relation of corpus to cervix), or an aplastic or infantile uterus, fibroids, prolapse, endometriosis, habitual abortion, or previous abdominal operations. This makes a real difference in certain categories, such as the sterilities, for many aplastic or infantile uteri are associated with sterility and almost all of these—all in this series, indeed,—are anteriorly placed and anteverted. Thus the incidence of retroversion in sterilities given here is really too high. The "normals" or "controls" are girls or women consulting me for such complaints as leucorrhœa, dyspareunia, frigidity, obesity or as desiring contraceptives, and were all nulliparæ. There are very few observations in the litera-

ture indicating the actual "normal" occurrence of retroversion, it appears.

From these data it will be seen that retroversion is "normal" for one woman out of every four. This is just the conclusion that Melhado and Smith reached. Curiously enough,

TABLE I.

Type of case	*Number of patients*	*Percentage in anteversion*	*Percentage in retroversion*
"Normal"	140	74	26
Backache	60	80	20
Dysmenorrhœa ..	157	81	19
Menorrhagia	116	87	13
Sterility	95	75	25
Amenorrhœa	33	79	21
Oligomenorrhœa ..	39	79	21

there was the same incidence of retroversion in the group of sterility patients as in the "normals", although the figure for the sterilities should be considerably lower, as has been indicated. It is still more remarkable, in the light of an all too widespread opinion among physicians, that the lowest incidence of retroversion was in the dysmenorrhœa and menorrhagia groups. Actually, retroversion was only half as common among women with menorrhagia as among normal women. Now if that points to any surgical therapy at all (which Heaven forefend!), it would urge one, not to suspend uteri for menorrhagia, but to sew them into retroversion! And we should cut those round ligaments for dysmenorrhœa, not plicate them! There is a famous remark of the comic character, Si Perkins, that might be quoted at this juncture: "It aint not knowin' that makes so much trouble; it's knowin' so much that ain't!"

RETROVERSION IN OBSTETRICS

Almost every post-partum woman is warned by her conscientious accoucheur nowadays to lie on her abdomen occasionally during her puerperium. That is meant to keep the uterus from falling into retroversion, for retroversion is so trouble-provoking! If the womb does become retroverted the "monkey-walk" or knee-chest exercises are usually advised. Is this rational? In order to discover the answer, I have gone through my obstetrical records and taken from them 94 unselected women having 117 pregnancies. All of these I had had an opportunity to examine before and after pregnancy or series of pregnancies. The following Table gives the results:—

TABLE II.

Anteverted before pregnancy	*Percentage unchanged by the pregnancy*	*Retroverted before pregnancy*	*Percentage unchanged by the pregnancy*
88 cases	89	29 cases	62

It appears, therefore, that pregnancy by itself only occasionally alters the position of the uterus. That would be expected, of course, if whatever uterine position she is first found to have is characteristic for each woman, and if uterine position is quite unimportant in relation to pregnancy. It is of interest that in this series there were almost four times as many chances of pregnancy spontaneously correcting a retroversion as of causing it!

But retroversion has been blamed for abortion and miscarriage, and, on occasion, for incarceration of the gravid uterus. Now incarceration is so rare that one almost never sees a case reported. For example, in the past 10 years, only one has been reported in English, and about 16 others throughout the world. The late Professor J. B. DeLee, who had perhaps the largest experience, both as a consultant and practising obstetrician, of any man in America, told me he had never seen a case of incarceration. Certainly I have never seen it in my meagre experience, and I have been ignoring retroversion for ten years. I have seen several women abort promptly, however, after their well-meaning obstetricians had inserted pessaries in order to "correct a retroversion"!

In 84 cases of spontaneous abortion only 27% showed retroversion of the uterus before or just afterward. Of 26 true habitual aborters 8, or 31%, had retroverted uteri before and after their abortions.[8] It will be seen that the incidence of retroversion in spontaneously aborting women is no higher than the normal expectancy if the one-quarter of women who are normally retroverted conceive as readily as their anteverted sisters. It does appear to be somewhat more frequent in habitual aborters, but every obstetrician knows how poor are the therapeutic results achieved by correcting such retroversion in this type of patient. It would seem, therefore, that the cause of habitual abortion can scarcely be related to the retroversion.

TABLE III.

No.	*Pre-operation complaints*	*Operation*	*Result*	*Uterine position now*	*Effect on fertility*	*Assessment of results*
(1)	Dysmenorrhœa and menorrhagia	Cyst of ovary; appendectomy; suspension	Pain cured; oligomenorrhœa	Anterior	?	Good
(2)	One abortion; menorrhagia; and dysmenorrhœa	Cyst of ovary; appendectomy; suspension	No change	Anterior	A child since	Bad
(3)	Menorrhagia and dysmenorrhœa	Appendectomy; suspension	No change	Retroverted	2 children since	Bad
(4)	Dysmenorrhœa	Cyst of ovary; appendectomy	No change	Anterior	Now pregnant on thyroid after 8 years' sterility	Bad
(5)	Dysmenorrhœa and irregularity	One ovary out; appendectomy; suspension	Regular; much less dysmenorrhœa	Anterior	Child since	Good
(6)	Chronic appendix and dead premature; and dysmenorrhœa	Cyst of ovary; suspension	No change	Anterior	Sterile since	Bad
(7)	Dysmenorrhœa	Curettage; later appendectomy; suspension	Dysmenorrhœa and menorrhagia	?	2 children	Bad
(8)	?	Curettage; suspension	?	Anterior	1 child	?
(9)	Dysmenorrhœa and menorrhagia	Appendectomy; suspension	Same	Anterior	1 criminal abortion	Bad
(10)	?	Cyst of ovary; appendectomy; suspension	Irregular since	Anterior	1 child	?
(11)	Sterility; dysmenorrhœa	Cyst of ovary; suspension	Same dysmenorrhœa + backache	Anterior	2 children	?
(12)	Dysmenorrhœa and menorrhagia	Appendectomy; suspension	Same	?	Sterile	Bad
(13)	Backache	Suspension	Same	Anterior	1 child	Bad
(14)	Dysmenorrhœa	Suspension	No dysmenorrhœa but bad backache	Anterior	....	?
(15)	Menorrhagia and dysmenorrhœa and sterility	Cyst of ovary; appendectomy; suspension	Menorrhagia worse	Anterior	Sterile; one intestinal obstruction since	Bad
(16)	Menorrhagia and dysmenorrhœa	Appendectomy; suspension	Same + bad backache	Anterior	Hernia in scar. Another laparotomy and a piece off ovary. 1 child	Bad
(17)	Hysteroid	Ovary out; appendectomy; suspension	?	Anterior	2 children	?
(18)	Menorrhagia and irregularlty and sterility	Appendectomy; suspension	Cured	Anterior	Sterile	Fair
(19)	?	Suspension	?	Anterior	Later operation for adhesions, ovary, tubes and appendix out. Sterile	Bad
(20)	Backache and headache	Cyst of ovary; suspension	No change	Anterior	Sterile	Bad

TABLE III—*Continued*

No.	*Pre-operation complaints*	*Operation*	*Result*	*Uterine position now*	*Effect on fertility*	*Assessment of results*
(21)	?	Suspension	?	Anterior	?	?
(22)	Menorrhagia	Ovary out; suspension	No change; below par	Anterior	....	Bad
(23)	?	Sterilization; suspension	Backache	Anterior	....	?
(24)	Headaches	Suspension	Cured	Big fibroids to navel	....	?
(25)	Backache due to hemi-vertebra	Cyst of ovary; suspension	No change	Anterior	Sterile	Bad
(26)	Leucorrhœa and menorrhagia	Curettage; appendectomy; suspension	No change	Anterior	....	Bad
(27)	Abdominal pains	Appendectomy; and suspension later	No change	Retroverted	Cured by thyroid	Bad
(28)	Menorrhagia and dysmenorrhœa	Suspension	Worse, so x-ray menopause	Retroverted	....	Bad
(29)	Abdominal pains	Cyst of ovary; appendectomy; suspension	No change	Anterior	Sterile	Bad
(30)	Dysmenorrhœa and backache	Endometriosis of ovary; suspension	Cured 2 years, then same as at first. Cured by x-ray.	Anterior	....	?
(31)	Sterility	One tube out; suspension	Many intestinal obstructions	Anterior	Sterile	Bad
(32)	Dysmenorrhœa and menorrhagia	Suspension	No change; cured by thyroid	Retroverted	1 child	Bad
(33)	?	Appendectomy; cyst of ovary; suspension	?	Anterior	1 abortion, then relative sterility	?
(34)	Menorrhagia; sterility	Herniotomy; suspension	Menorrhagia worse and severe dysmenorrhœa	Too far anterior	Sterility	Bad
(35)	Menorrhagia and metrorrhagia	Appendectomy; suspension	Menorrhagia and metrorrhagia worse; dysmenorrhœa	Retroverted	Sterile	Bad

THE SUSPENSION OPERATION

What happens to women who have retroverted uteri surgically "suspended"? The following Table lists all those I have seen in the past ten years. Many of these have consulted me for nothing that could be related to their operation, but as a matter of interest they are included with the rest. It may be objected that the more satisfactory cases would not consult a physician again, but I suspect that this really is a fairly representative cross-section of such a post-operative group!

In these 35 cases the result could be classified as bad in 22 and good in only 2. There was recurrence of the original retroversion in 5. Sterility ensued in 13, and not all the 35 were married! Severe backache ensued in 4. Intestinal obstruction ensued in 2, and a hernia in the scar appeared in 1. Many of these operations had been done by the best surgeons in the country. What greater indictment of an operation could there be? If anything more were needed to indicate the general dissatisfaction with the results of the operation, even among those who perform it, it would be the numerous surgical devices described for it. One suspects they are all not only needless but that many actually produce vicious results! How often at laparotomy the "adherent retroverted uterus" is lifted up with the greatest ease! Vaginal

examinations indicate rather inadequately whether the retroversion is or is not "adherent". I have heard recently of an unmarried girl dying after an operation for retroversion. The operation was performed because she was assured by a gynæcologist that she would be sterile in her impending marriage!

Rendle-Short[9] well says: "The successful results of various operations for backward displacement can be divided into two classes: first, those which are an anatomical success, the uterus being in the anteverted position on examination; and, secondly, those which are also cured in the matter of symptoms—subjective success. It has been found that these two do not always go together." She found 79% of 92 women operated on for retroversion had a perfect anatomical result: 9% were cured as regards symptoms, despite a recurrence of the retroversion. In 8% more the retroversion had recurred and the symptoms were the same or aggravated; 58% of 19 sterility cases were cured. Two of three habitual aborters were helped. She concluded that the operation might with some justification be advised for intractable sterility!

CURES

Many conscientious physicians know of women who have been cured of their pelvic complaints by the use of a pessary or uterine suspension. What shall we say of these?

I have seen some of these, and my experience coincides with that of Professor Donald. Often there was relief, while the retroversion still persisted, whether or not the pessary was still in the vagina. Oftener still, there never had been a retroversion, or the uterus was so mobile that its position must have varied several times a day. On occasion, I have removed such a pessary, allowed a retroversion to recur, treated the woman by some more rational means, such as by giving her pelvis short-wave treatment for uterosacral cellulitis, or thyroid extract for a menorrhagia or œstrogenic dysmenorrhœa, and seen her symptoms relieved completely, the recurrent retroversion notwithstanding. It should be of interest that an obstetrician and gynæcologist can successfully ignore retroversion for ten years.

The normal uterine corpus weighs very little and could not cause "pressure" by any stretch of the imagination. Certainly it could not weigh as much as a full rectum nor produce as much pressure on the subjacent lumbosacral nerve roots. Why hasn't somebody thought of "suspending" the rectum to relieve chronic backaches?

Where endometriosis or fibroids or uterosacral cellulitis cause backaches let us correct the cause and ignore any incidental retroversion that may co-exist. Pessaries do occasionally relieve backache in pelvic inflammatory conditions by letting the cervix drop back as the fundus is pushed ahead. This lessens the tension on the inflamed uterosacral ligaments. Is it not more rational to melt the cellulitis away with pelvic heat than to insert a pessary?

Regarding "cures" by suspension I recall seeing a case of tic of the 9th cranial nerve. This woman was cured for two years by a perineorrhaphy!

SUMMARY

1. The amazing development of the idea that uterine retroversion causes pelvic complaints *per se* is considered.

2. A series of unselected cases is reviewed to show that the incidence of retroversion in dysmenorrhœa and especially in menorrhagia is actually less than the one in four incidence of retroversion in "normal" women. Even women having sterility or backache show a lower incidence of retroversion than normal.

3. Pregnancy only occasionally alters uterine position, and, when it does so, is nearly four times as apt to correct a retroversion as to produce it.

4. Uterine incarceration is very rare. There were approximately 17 cases reported in the world's medical literature in the last ten years.

5. The incidence of retroversion in abortions is not abnormal.

6. An unselected series of 35 uterine suspensions is reviewed. The results were deplorable with few exceptions.

7. The "cures" following the correction of retroversion are considered critically.

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THE WEATHER AND THE PATIENT'S SKIN*

By Norman M. Wrong, M.D.

Toronto

"WEATHER is a literary specialty and no untrained hand can turn out a good article on it." So spoke a literary gentleman many years ago and, as I do not consider myself a literary specialist, I will say little about the weather and much about the patient's skin.

The effects of weather on the skin will be discussed under four heads. (1) The effects of cold. (2) The effects of heat. (3) The effects of low humidity. (4) The effects of sunlight and general "weathering". I propose to deal chiefly with the first and the last of these.

EFFECTS OF COLD

The effects of cold have been studied extensively by Lewis and his co-workers, and the effects of long-continued cold—which is what we are really interested in—have been set forth at length by Haxthausen,[1] of Copenhagen. From an experimental standpoint, slight cooling causes a contraction of the capillaries, venules and arterioles, but more extreme cold causes a dilatation of the minute vessels and a contraction of the larger arterioles, producing a reddish skin with a tendency to cyanosis. This is the underlying pathological change in the following: (*a*) chilblains, or erythema pernio; (*b*) erythrocyanosis crurum puellaris; (*c*) acrocyanosis; (*d*) livedo reticularis; (*e*) trench feet.

(*a*) *Chilblains,* or erythema pernio, was known and described by Hippocrates and Celsus. In countries where the condition is rampant it is said that every physician and every family have their own pet cure, so suggesting that all are useless. It is a very rare disease now among urban dwellers in Canada, and the reason is found in central heating. Where this form of heating has been instituted in girls' schools in England, chilblains have disappeared, proving that the cold floors and cold draughts of stove and fireplace heating are the cause of this condition. The cure is evident, but not always practical. Chilblains occur most commonly on the hands and feet as round or oval lesions with a peculiar bluish red colour. The parts are swollen, hot and tense and, when pressed, the colour leaves, to reappear slowly. In more severe cases, there are bullæ and may be ulceration. The itching is very intense when the patient comes from the cold into a warm room.

(*b*) *Erythrocyanosis crurum puellaris.*—This disease, as its name implies, affects young women exclusively, usually on the legs, although its appearance on the thighs, forearms, and arms has been described. An intense bluish red colour on the outer aspect of the lower third of the legs is usually seen. Fine, dilated venules appear with this background of bluish red colour, and the whole area is thickened and hard. In addition, keratotic plugs in the follicles are seen, similar to the appearance in keratosis pilaris. There are few symptoms, and the main complaint is the appearance. It is usually worse in the winter, improving in the summer, and becoming less with advancing years.

(*c*) *Acrocyanosis.*—In this disease, which is most commonly found in women, the striking feature is the bluish red colour of the dorsa of the hands and feet. When the skin is pressed, a white area is left which only slowly regains its colour. The extremities are very cold, and there is often an accompanying pasty thickening of the skin. Frequently, hyperhidrosis accompanies this condition.

(*d*) *Livedo reticularis.*—This marbling of the skin is seen commonly on exposing any patient's skin in a cold room, only to disappear when the skin is warmed. It persists in some patients, particularly adolescents. This same marbling or retiform appearance is seen after exposure to light, heat, and to some chemicals.

(*e*) *Trench feet.*—This condition, which was so prevalent during the last war and is happily unknown in this one, is really a transitional stage between frostbite and chilblains. There is usually a sensation of burning in the feet, followed by œdema of the feet and legs, and even thighs. This is accompanied by cyanotic redness, hæmorrhagic bullæ and ulceration. This disease is produced by a combination of cold, stasis, and dampness, usually accompanied by fatigue. The control and treatment are evident.

Cold which is more severe than that which produces the above conditions results in frostbite. According to Haxthausen, the skin temperature must be depressed below –6° C., to produce necrosis of tissue and ulceration. Higher temperatures than that may result in bluish

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* Read at the Seventy-third Annual Meeting of the Canadian Medical Association, Jasper Park, Alberta, June, 1942.

From the Department of Medicine, University of Toronto.

redness and tingling, or even in bullæ, but not actual necrosis. The critical point seems to be –6° C., and the effect is probably on the vessels. Frostbite will not be discussed at length except to say that, if the hands are affected, the thumb is usually spared, but, if the feet are affected, the great toe may be the worst victim. This is seen in fliers who suffer from frostbite at high altitudes.

In addition to the above-mentioned effects of cold there are others which are less understood, but, from the patient's standpoint, are equally important. These are: (1) cold urticaria; (2) prurigo hiemalis or winter itch; (3) dermatitis hiemalis or winter eczema.

Cold urticaria.—The mechanism of the production of this condition is not well understood. In these patients the reaction of the skin to other stimuli is usually normal, but urticaria is produced on exposure to cold. The skin eruption may be associated with œdema of the larynx and with syncope and death, and the phenomenon is undoubtedly the cause of some cases of drowning. Some cases are associated with paroxysmal hæmoglobinuria and with leucopenia.

Prurigo hiemalis.—This distressing complaint is often associated with mild degrees of ichthyosis and occurs in both sexes, at all ages, but is particularly severe in the aged. It starts in the fall and, the colder the weather, the worse the itch. There is nothing to be seen except the associated dryness, until secondary lesions appear from rubbing and scratching.

Dermatitis hiemalis, or winter eczema. This appears suddenly with the first cold snap in the winter and may last until spring. It is most evident on the hands, forearms and arms, but may occur on the legs. These lesions are well defined and ringed with vesicles at the periphery, which dry to form crusts. Niles,[2] of New York, suggested a prescription for an ointment which he found very efficacious in this condition.

The effect of heat will not be discussed at length. Everyone is familiar with the effects of sunburn and thermal burns.

Low Humidity

The effects of low humidity will be dealt with only briefly. I have had the impression for some time that low humidity in houses and offices was one of the great factors in contributing to excessively dry skin and to winter itch and winter eczema. In a casual survey of the literature, this impression has not been borne out. Yaglou,[3] of New York, does not favour artificial humidification, as he states that rarely does humidity fall below 20% in houses, due to moisture in furniture, walls, etc. This may apply to New York, but I do not believe it applies to the colder parts of Canada. With an outside temperature of 40° below zero, Fahrenheit, and the house or office heated to 80° above, the humidity must be closer to 5 than 20%, with a consequent drying effect on skin and mucosa.

McConnell[4] found in a survey of 10,000 employees, one-half of whom were in air-conditioned offices, that there was no difference in absenteeism from illness between the two. Air-conditioning in the summer time should aim at only slight lowering of temperature as compared with outside, but a marked lowering in humidity. In that way, the contrast on returning to the outdoors is not too great. Comfort in summer or winter depends on: (*a*) air temperature; (*b*) humidity; (*c*) air movement, which should be at least 15 ft. per min.; (*d*) radiation from the skin; (*e*) cleanliness. Simple readings from a dry-wet bulb thermometer are not sufficient when there are all these factors to consider.

Sunlight and "weathering".—The effect on the skin of one exposure to sunlight is erythema with scaling and and probably pigmentation. The effects of hundreds of short or long exposures over a period of years are many and varied. A condition results of premature ageing in which the exposed skin becomes pigmented, thickened, leathery, and, in addition, hard, horny growths may appear. This is the so-called sailors' skin, which is seen as often in farmers as in sailors, or in anyone who is outdoors in all weather. The darker the skin, the less the tendency to the appearance of these horny growths. In Australia the Anglo-Saxon works in the fields and plays on the beaches, and the incidence of keratoses and skin malignant growth is very high: it is said to be the highest in the world. The Italian workers imported into Australia years ago show a much lower incidence of these two conditions. Paul,[5] quoted by Goldsmith, emphasizes the great importance of chronic solar dermatitis which resembles mild x-ray dermatitis in the production of precancerous lesions, particularly the

senile keratosis. In addition to being seen so commonly in Australia, changes in the skin due to sunlight are seen very often in the southern States and western Canada and commonly, in eastern Canada. Of 125 consecutive cases of malignant tumours of the skin seen at the Ontario Institute of Radiotherapy, Toronto, 108 were on the face, ears, neck, or dorsa of the hands, *i.e.*, on areas exposed to sunlight.

From an experimental standpoint, it has been found that repeated exposure to strong ultra-violet light raises the cholesterol content of the skin in the area treated, and cholesterol is closely allied chemically to one of the carcinogenic agents. Colquhoun, of Melbourne, reported a case of multiple keratoses on the chest of a man who had been treated with quartz light for 18 months. Hewer[7] described several cases of multiple epithelioma in albinos of dark races much exposed to sun. Goldsmith[6] says that the senile keratosis which occurs on the skin exposed to much weathering is the commonest precancerosis, and Hookey[8] says that 25% of them become malignant. Skin cancer is, I believe, almost unknown in the Eskimo, so it would seem that strong sunlight has much more of a carcinogenic effect than extremes of cold and wind. The commonest sites for skin cancer are the face, lips, neck, ears and dorsa of the hands; that is, areas which are exposed to most of the "weathering". I doubt whether the vogue for sun-baking will increase the incidence of carcinoma on other areas of skin, as it is done for such a short time each year. Aitken[9] believes that pigment in the skin protects more against the luminous rays than ultra-violet rays and shows data to prove his contention.

In addition to senile changes in the skin, keratoses, and carcinoma, sunlight produces other effects. One of the most striking of these is light urticaria. This is like cold urticaria in that the mechanism is not understood and the response to other stimuli is normal. There are some skin diseases which seem to be aggravated by or precipitated by sunlight. Notable among these are lupus erythematosus, erythema multiforme, and rosacea.

Sun-bathing in moderation is a great adjunct to health, but the effects of sun-baking may be definitely harmful. Sunlight in excess undoubtedly causes skin disease and probably is the chief cause of skin cancer.

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RÉSUMÉ

Le froid, la chaleur, la sécheresse du milieu, l'exposition au soleil et aux intempéries affectent la peau à divers degrés. Les effets du froid sont bien connus. Les principaux sont l'érythème pernio, l'érythrocyanose crurale des jeunes filles, l'acrocyanose, la lividité réticulaire et les *pieds de tranchées*. Ces états sont amenés par des contractions ou des dilatations excessives des capillaires. Les effets de la chaleur ne sont pas discutés. La sécheresse du milieu ambiant assèche la peau et cause, pendant l'hiver, des démangeaisons et des eczémas. La climatisation de l'air des appartements n'améliore pas beaucoup la situation. Le confort véritable dépend plutôt de la température de l'air, de son humidité, de son mouvement, de l'évaporation cutanée et de la propreté. L'exposition prolongée au soleil et aux intempéries provoque le hâle et prédisposerait au cancer de la peau. JEAN SAUCIER

NON-MALIGNANT DISEASE OF THE GALL BLADDER AND BILE DUCTS*

By L. G. McCabe, M.D., F.R.C.S.(C)

Windsor, Ont.

A NUMBER of theories have been advanced to explain gall-stone formation and gall-bladder disease, but so far, none of them are satisfactory, and the causation of these conditions remains obscure. For the last decade or two, the favourite theory has been that the process leading to gall-bladder disease was initiated by the invasion of the gall-bladder wall by some micro-organism of low virulence, which, apparently, had a selective affinity for this particular region. The non-hæmolytic streptococcus was considered to be most frequently the culprit and was supposed to make its way to the gall bladder by way of the blood stream, from its lurking places in teeth, tonsils or other "foci". Starting from this premise, a very plausible sequence of events was postulated: (1) the organism set up a low-grade inflammatory process in the gall-bladder wall; (2) this inflamma-

* From the Surgical Service of the Hotel-Dieu, Windsor, Ont.

tion caused the gall-bladder mucosa to lose its power of selectivity in absorption, and instead of removing only water and inorganic salts from the bile it also removed bile salts; (3) as bile salts are necessary to keep the cholesterol in solution, this abnormal loss of bile salts causes cholesterol to be precipitated and form gall stones.

This theory was based on the evidence of various experiments, from those of Rosenow in 1916 to those of Wilkie in 1927. There were, however, facts in the pathology of the gall bladder that this theory did not explain. In the first place, the pathological picture in early gall-bladder disease is not that of pyogenic inflammation. The infiltrating cells are predominately lymphocytes and wandering cells, and not leucocytes. Suppuration and ulceration are rarely found. Even in those cases that we call empyema of the gall bladder, what appears to be pus, if examined, will usually be found to be an emulsion of amorphous cholesterol, or of calcium carbonate, and it will seldom give any growth on culture. The fact that gall-bladder disease is found to be three or four times more frequent in women who have born children, than in men or in nulliparous women, is another difficult hurdle for this theory to jump. The more I see of gall-bladder disease, the more firmly I am convinced that infection is not the original cause of the process. Undoubtedly, however, infection becomes superimposed on gall-bladder disease in its later stages, especially when there is obstruction by stones in the main bile channels.

The older idea that stasis in the biliary stream is the cause of gall stones, is also difficult to support. The chief argument against it is that in those pathological conditions where stasis is greatest, we very rarely find stones. In cases where the common duct is obstructed by tumour growth in the head of the pancreas or in the ampullary region, we have stasis of bile in its most marked form, yet we scarcely ever find any gall stones or thickening in the gall-bladder wall, even though the gall bladder and duct system are tremendously distended with thick black concentrated bile. The best that we can do at the present time to explain the cause of gall bladder disease is to say that cholecystitis in 90% of cases is caused by the presence of stones, and that the stones are produced by some change in the chemistry of the bile that leads to the precipitation of cholesterol, or, more rarely, of bile pigment or calcium carbonate. What that change is we do not know, but we do know that pregnancy is one of the factors that predispose to it. In the 10% of cases of definite gall-bladder disease in which no stones are found some other explanation is necessary. In some cases stones have been present and have been passed into the intestinal tract before the surgeon has an opportunity to see the gall bladder. In a small percentage of them the reflux of activated pancreatic juice into the gall bladder in a high enough concentration to produce a chemical inflammation is a probable cause.

PHYSIOLOGY OF BILE FLOW

In discussing disease of the bile passages, one should keep in mind certain facts about the normal physiology of the gall bladder and the mechanics of biliary flow. The normal gall bladder is blue in colour, has quite a thin wall and contains fairly thick, very dark mucinous bile. The liver secretes continuously its thin watery golden yellow bile, which is forced up the cystic duct into the gall bladder, by the resistance of the papillary sphincter, except at such times as the latter muscle is relaxed. The flow of bile from the ducts and gall bladder into the duodenum is controlled by reciprocal innervation with sympathetic and parasympaethic nerve supply. The adequate stimulus which relaxes the sphincter of Oddi and initiates the outflow of bile through the papillary opening is the presence of food, especially fats, in the duodenum.

The gall bladder concentrates the liver bile by absorbing water and salt (normal saline) from it, so that the normal gall bladder with a capacity of 50 c.c. can accommodate up to 500 c.c. of liver bile, returning the 450 c.c. of saline to the blood stream through the lymphatics. In considering gall bladder disease, it is important to keep in mind this double route by which the contents of the gall bladder escape. Any obstruction to either avenue of exit will cause serious consequences.

The wall of the fundus of the gall bladder is very sparsely supplied with muscle, having no continuous muscular layer, but only scattered fibres, and is not able to empty itself entirely. The muscular element of the bile passages is located chiefly at two points: (1) the gall-bladder neck and upper two-thirds of the cystic duct; (2) the ampullary region of the common

duct. The more violent pain of biliary colic is caused by a stone being grasped by the muscular wall at these locations.

PATHOLOGICAL CHANGES

The earliest evidence of a departure from normal that one sees in the gall bladder is that condition commonly called the "strawberry gall bladder", in which the mucosa is studded with small yellowish spots arranged in an indefinite, linear formation. These yellow specks are small particles of cholesterol deposited in the tips of the villous-like folds of the mucosa of the fundus, and they cease abruptly at the junction of the fundus and the gall-bladder neck. Why the cholesterol becomes deposited in this manner is not known, but one may surmize that it is an attempt on the part of the gall-bladder mucosa to forestall a threatened formation of gall stones, by seizing in a phagocytic manner, cholesterol crystals that have made their unwelcome appearance in the gall bladder bile. This view is strengthened by the fact that cholesterosis is never found in any, other than a comparatively normal gall-bladder mucosa, and no doubt it frequently disappears as the defense effort on the part of the mucosa succeeds in preventing stone formation. It is never found in advanced gall-bladder disease, as if the mucosa, having definitely lost the battle to prevent gall stone formation, makes no further attempt to seize the intruding crystals.

Cholesterosis, of itself, causes no symptoms. The surgeon sees it usually associated with a few small, recently formed, mulberry stones in a patient with a comparatively short history of attacks of gall-stone colic. When cholesterosis with or without stones is found at operation, the proper treatment is the removal of the gall bladder. One might argue against this advice, that in the case of cholesterosis without stones the gall bladder may still return to a normal state and should not be removed. However, as the surgeon has operated only for definite symptoms, that is, for one or more attacks of gall-stone colic, he may assume that stones have already been present and passed down the ducts, and that, therefore, the gall-bladder disease has proceeded beyond the point at which a return to normal is probable.

With the formation of stones in the gall bladder the patient commences his, or, more frequently, her, career as a case of gall-bladder disease, a career that usually extends over a number of years and may be stretched out from adolescence to ripe old age. Up to the point where some of the more serious complications intrude themselves, the symptoms of gall-bladder disease may be discussed under three headings: (1) gall-stone colic; (2) the acutely obstructed gall bladder; (3) indefinite digestive disturbances.

In the classical case of gall-bladder disease the first symptom is an attack of gall-stone colic, caused by one or more of the stones lodging in the neck of the gall bladder or the cystic duct and causing violent spasm of the circular muscle in this region. The pain is severe and begins abruptly, often waking the patient in the middle of the night. While the onset is abrupt, it has not the dramatic suddenness of a perforated peptic ulcer. One should qualify the term colic as applied to this pain because it is not like the colic of intestinal cramps, where the pain entirely disappears between spasms. In gall-stone colic, the pain rises to a crescendo of severity, and then moderates, but does not cease. In contrast to the motionless state of the patient with perforated peptic ulcer or with coronary occlusion, the patient with gall-stone colic is apt to squirm about or walk the floor. In true gall-stone colic, there is no tenderness to palpation, or rigidity of the abdominal muscles. It is pure visceral pain and is felt in the centre line, high in the epigastrium, the location of visceral pain for those organs that derive their autonomic nerve supply from the cœliac plexus and their blood supply from branches of the cœliac artery.

DIFFERENTIAL DIAGNOSIS

Perforated ulcer, coronary thrombosis and *tabetic crises* are the three most likely conditions to be confused with gall-stone colic. The extreme rigidity in perforated ulcer, the ulcer history in most cases, in contrast to the history of previous gall-stone attacks, the shoulder-tip pain so often present in perforated ulcer, never in gall-stone colic, will usually suffice to distinguish between the two conditions.

Coronary disease is most frequent in males over 50, while gall-bladder disease is most frequent in females under 50. The distribution of the pain through the centre of the chest, in the mid or upper sternal region and radiating to the arms, the grey face and anxious expression, the complete immobility, the pericardial fric-

tion rub, all will usually enable us to recognize the coronary accident. A routine check of the reflexes should never be neglected in any visceral type of abdominal pain, and may save the embarrassment of opening the abdomen for a tabetic crisis.

Acute appendicitis and *acute small bowel obstruction* are less likely to be confused with acute gall-bladder disease. The local symptoms in acute appendicitis and the absence of a history of previous gall stone attacks will be sufficient distinction in most cases. It is true that both conditions commence with a central visceral type of pain, and, if they progress, change to a right-sided somatic pain of parietal peritoneal irritation, but the shift is a matter of hours in acute appendicitis and of several days in the acute gall bladder. The age of the patient is helpful in a one-sided way, because gall-bladder disease is rare under 30 years, while appendicitis is common to all ages. In acute small bowel obstruction, the type of "colic", as noted previously, is different. This and the persistent vomiting, the increasing distension, and the much more rapid progress to a very sick appearance will usually leave no doubt as to the diagnosis.

There is one type of small bowel obstruction that deserves special mention, because it is secondary to gall-bladder disease, when a large gall stone ulcerates from Hartmann's Pouch into the duodenum. This patient will usually be an elderly female with a long history of gall stone attacks, and, while this time the pains are different, she hesitates to call the doctor because she thinks she will be well in 4 to 5 days, as on many previous occasions. The doctor often delays a day or two for the same reason, and it is remarkable how these cases so often come to operation about the 6th or 7th day, with a mortality of about 60%.

The attack of gall-stone colic may cease as suddenly as it began, as a result of the stone passing through the muscular part of the cystic duct, or falling back out of the gall-bladder neck. In that case the patient is quite well, almost immediately, and can go about his activities as usual. When not relieved in this way, and the obstruction in the cystic duct continues, the acute spasms of pain gradually subside after a few hours, because the circular muscle of the cystic duct or gall-bladder neck tires out. The symptoms then merge into those of the acutely distended gall bladder, a steady deep pain of moderate severity felt in the epigastrium and slightly to the right and through to the back in the region of the lower end of the scapula. At the same time the gall bladder frequently becomes palpable, as a moderately tender tumour mass that moves up and down on respiration. The pain in the back is always at or near the lower angle of the right scapula, and never at the shoulder tip, as some times stated in textbooks.

Shoulder-tip pain, accompanying acute abdominal symptoms, should make one suspect perforated ulcer, or at least that some irritating fluid is coming in contact with the parietal peritoneum, on the under surface of the central part of the diaphragm. This local pain at the lower angle of the right scapula, in the acutely obstructed gall bladder, is caused by the œdema around the gall-bladder neck spreading to and stretching the sensitive parietal peritoneum of the posterior abdominal wall immediately behind the bile ducts. Œdema is the most prominent feature of the acutely distended gall bladder, and as it increases in the narrow region of the gall-bladder neck the circulation in the fundus becomes impaired and patches of gangrene appear in the gall-bladder wall. Infection then becomes superimposed on the obstructed state, and involvement of the parietal peritoneum of the anterior abdominal wall is made evident by a marked increase in the degree of tenderness and the development of rigidity in the upper right abdominal musculature, accompanied by some fever and a sharp rise in the leucocyte count. These are warning signs that surgical intervention should be no longer delayed, for fear of rupture. The extent to which a gall bladder will enlarge during such an attack will be in inverse ratio to the amount of thickening and fibrosis in its wall, as the result of previous attacks.

LATER EFFECTS ON GALL BLADDER

When a gall bladder has been through a number of these obstructive attacks, it is inevitable that chronic infection in the gall-bladder wall and neighbouring lymphatics becomes a more and more important factor in the pathological picture. Neighbouring structures become involved in peri-cholecystic inflammation; the duodenum and sometimes the pylorus, the transverse colon, and the omentum will become adherent to the gall bladder and eventually all become involved in a dense inflammatory mass, with

fibrosis of the neighbouring part of the liver. To the extent that these peri-cholecystic adhesions develop, the mechanics of digestion in the region of the pyloric antrum and the duodenum will be interfered with, and digestive disturbance will be a more continuous symptom. The earlier stages of gall-bladder disease are, in my experience, remarkably free from digestive disturbances, and I do not consider "flatulent dyspepsia" to be a symptom of gall-bladder disease unless the patient gives a history of having had one or more acute gall-bladder attacks.

We should do our utmost to bring gall-bladder disease to operation before the more advanced stages are reached. Otherwise not only will the technical problems in the operation be made more difficult but permanent damage through fibrosis to the motility of the pyloric region and permanent liver damage may render the results of operation less satisfactory. Any patient who has had more than one attack of gall-stone colic, and any patient who has an attack from an acutely obstructed gall bladder should be advised to have operative treatment, unless there is some very serious reason that makes him a poor operative risk. The question of operating on the acute gall bladder immediately, or waiting for it to subside, has been debated quite briskly in recent years, and in general, opinion seems to favour immediate operation on the ground that the increased risk of operating during the acutely obstructed stage is much less than the danger of gangrene and rupture, while waiting for the acute attack to subside.

I am inclined to favour a compromise in this matter and to wait four days, then operate if the attack is not showing definite signs of subsiding at the end of that time. If it is definitely subsiding, a further delay of a week or two until the œdema in the gall bladder and neighbouring structures has had a chance to disappear will simplify the technical problem involved in removing the gall bladder. Any flare-up of the acute symptoms should be the signal to delay no longer. During this waiting period one must watch the patient very closely, because it is a well-known fact that under such circumstances the clinical symptoms, physical signs and laboratory data often fail to indicate accurately the course of the pathological process in the gall bladder. Gangrene and perforation may occur in a case that showed every indication of subsiding.

PROBLEMS OF OBSTRUCTION

Some of the most serious problems that confront the surgeon in dealing with gall-bladder disease are those associated with the presence of stones in the common or hepatic ducts. Obstruction to the free flow of bile through these main bile channels may be due to a variety of causes, the two most frequent being gall stones and new growths. Many years ago, Courvoisier contrasted the clinical and pathological picture accompanying these two types of obstruction. His description has been found true in such a large majority of cases that it has been called Courvoisier's law. Briefly stated, it is:

> "Where the patient has recurrent attacks of biliary colic, accompanied by chills and fever, and followed by jaundice, one will find the common duct obstructed by a stone, and one will also find the contracted thick-walled gall bladder of chronic cholecystic disease. On the other hand, when the obstruction in the common duct is due to a new growth, a painless afebrile jaundice, with no intermissions, becoming progressively deeper, and associated with a large and palpable gall bladder is the characteristic picture."

There are cases which do not comply with this law, but they are rare. In general, it will be found a safe guide in diagnosis. Less frequent causes of obstruction in the main bile passages are stricture, usually the result of operative trauma, and pressure on the duct from inflammatory swelling in the gall bladder or pancreas, or in the glands of the gastro-hepatic omentum.

Although it is undoubtedly a fact that gall stones may form wherever there is bile, most of the stones found in the common or hepatic ducts are originally cholesterol stones that have been formed in the gall bladder. If they remain in the common duct for any length of time, they will increase in size by the deposit on their surface of bilirubin calcium. In about 70% of cases of stone in the common duct, a single stone will be present, and if the patient is operated on during an attack of colic, it will be found impacted in the lower end of the duct. If the operation is during the interval between attacks, it may be found floating anywhere in the dilated duct system. The fact that these stones are approximately of the same specific gravity as bile, partly accounts for the intermittent character of the symptoms.

The trinity of symptoms of common-duct stones are biliary colic, jaundice, chills and fever, occurring usually in that order, and de-

scribed many years ago by Charcot as intermittent hepatic fever. The pain associated with a stone impacted in the lower end of the common duct is particularly severe. It is a true visceral pain, unaccompanied by tenderness, and is felt in the centre line, high in the epigastric region. When the attack has continued for some time the periductal and pericholecystic œdema may produce a certain degree of irritation to the parietal peritoneum and a moderate degree of tenderness and rigidity will be present. However, it is a good rule to keep in mind, that if an attack of severe epigastric pain is accompanied in its early stages by marked tenderness on palpation, and rigidity of the overlying muscles, the patient is probably suffering from something other than gall-stone colic.

About 75% of patients in whom stones are found in the common duct at operation will have given a history of jaundice. In most cases there is also a history of previous attacks of colic without jaundice, indicating an earlier stage, when the disease was confined to the gall bladder and cystic duct. The character of the attack in common-duct obstruction by stone will depend to some extent on the condition of the gall bladder. If that organ is fairly healthy and functioning well, jaundice will be much slower in making its appearance following the attack of colic, as the gall bladder by its concentrating function can take care of the biliary output for several days, and by that time the stone may be released from its impacted position, and the free flow of bile resumed. More frequently, however, when there is a stone in the main duct system, the gall-bladder function has been largely destroyed by long standing cholecystic disease, and jaundice makes its appearance within twelve to twenty-four hours after the initial attack of colic. The main bile ducts cannot harbour a stone for long without becoming infected, and this accounts for the third in the triad of symptoms, the fever, which is likely to be of the nature of a rapid rise, with a chill, to be followed by a drenching perspiration as the temperature falls.

INDICATIONS FOR EXPLORING THE COMMON DUCT

A large experience with gall-bladder surgery will demonstrate the fact that quite often there are stones in the common duct which have not yet produced the typical symptoms usually associated with that condition. These are small stones that float in the bile stream in the main duct system, and have produced no obstruction. If overlooked at operation, they will very frequently increase in size and cause obstruction and infection at a later date. Such stones in the common duct overlooked at operation are the most common cause of recurrent symptoms following cholecystectomy for gall bladder disease. The appreciation of this fact has led most surgeons to explore the common duct when operating for gall-bladder disease much more frequently than had formerly been considered necessary. What are the indications that should guide us in making a decision on this important point? (1) Obviously when stones can be palpated through the duct wall. (2) When there is a history of jaundice. When a patient has gall-bladder disease with or without stones in the gall bladder, and has at any time had jaundice following an attack of colic, one must take for granted that there are stones in the common or hepatic ducts, until it is proved otherwise by a thorough exploration. (3) When the common duct is unduly dilated, or is thick-walled and white, instead of thin and blue, as the normal duct should be. (4) When the cystic duct is unduly dilated, thereby implying that something other than bile has passed through it. (5) When the gall bladder contains small stones or biliary mud it is to be presumed that such contents will have made its way down even a normal cystic duct; true, in most such cases it will pass on into the duodenum, but one cannot count on such an outcome. A mass of mud and small stones left in the lower end of the common duct may later solidify into a good-stized stone that will cause obstruction.

In order that this last indication should not be overlooked, it should be made a rule that whenever a gall bladder is removed, it should be handed to someone in the operating room to open it and present it for the surgeon's observation as to its contents and the state of the gall-bladder wall. In not a few cases the decision on the matter of exploring the common duct will depend on this examination.

While these five indications for exploring the common duct for stone are fairly definite, there are other imponderable factors which will affect one's decision. The longer the patient has had symptoms of gall-bladder disease, the more likely it will be that stones or infection will be found

in the main duct system. This fact is the strongest argument for early surgical interference when the disease is confined to the gall bladder itself, and the main bile channels are clear. Under such circumstances, the mortality of gall-bladder surgery is not greater than 2 or 3%. Once stones enter the common duct, infection of the whole duct system, extra- and intra-hepatic, very soon follows, with damage to liver function of greater or less degree, depending on how long the condition is permitted to continue without surgical relief. Under such circumstances, there will be a sharp rise in operative mortality and morbidity, a rise that is chargeable not to the surgical procedure itself, but to the delay that ensued before surgery was instituted.

In dealing with these long-standing cases of common duct obstruction and infection it is forunate for both the patient and the surgeon that nature has provided a wide margin of safety in the enormous physiological reserve of liver. Experimentally, 70% of a dog's liver can be removed without producing any symptoms of liver insufficiency. This margin of safety is increased in the case of chronic liver damage by the fact that the liver cells possess great powers of regeneration. These facts explain why inflammatory processes in the main duct system can go on for many years, with the patient remaining in good enough health to refuse operation, being content to go through the occasional attack of colic, chills and fever, with or without jaundice. Then after a particularly severe attack, the acute symptoms do not subside, the jaundice persists and he is handed over to the surgeon, and presents a most difficult problem, because we cannot know for certain to what extent his liver reserve is depleted. The tolerance to obstruction of the main bile duct varies a great deal in different individuals, a fact that makes it difficult to foretell the extent of liver damage that will be present in any particular case. Various tests of liver function have been designed to give us this information, but none of them are very accurate or reliable. We are often forced to operate on the patient with long-continued common-duct obstruction, knowing that the risk is grave, but knowing also that it will probably never be any better. Fortunately, a good proportion of such cases stand operation better than we had reason to expect, and I do not think that we should refuse operation in case of obstructive jaundice on the basis of results of any of our present tests of liver function. Patients with poor renal function, with casts in the urine, and a high non-protein nitrogen are bad risks. The jaundiced patient who is mentally confused or irrational is distinctly a bad risk.

Certain preoperative measures are essential to assure these patients the best chance of surviving operative procedures. (1) Build up an adequate glucose reserve by the intravenous administration of 5 or 10% glucose solutions. (2) Several blood transfusions, before operation. (3) Administration of vitamin "K" and bile salts, to overcome the tendency to hæmorrhage that has been one of the chief dangers in operating on jaundiced patients. Since Quick and his associates demonstrated that the hæmorrhagic tendency in jaundiced patients is due to a deficiency of prothrombin in the blood plasma, and Dam and his associates that this deficiency can be corrected by administration of vitamin "K" and bile salts, the danger from hæmorrhage in jaundiced patients has been greatly diminished.

The recurrence of attacks of gall-stone colic after operation for gall-bladder disease will in most instances mean that stones have been overlooked in the duct system, either from failure to explore a common duct that contained stones, or failure to remove all of the stones in cases where multiple stones were present. We have noted that in one-third of cases of common-duct stone, more than one stone is present in the main duct system. The number may run as high as several hundred, in cases where a gall bladder that is full of small stones gradually contracts, due to fibrosis in its wall, and forces its contents along a dilated cystic duct and fills the common, the common hepatic, and the hepatic radicals to their second or third divisions with a mass of stones, through which the bile makes its way like water through a coarse gravel filter. To remove all these stones from the hepatic ducts is a difficult problem.

Operative Mortality

The operative mortality in non-malignant gall-bladder disease varies a good deal in statistics from different institutions. In the Hotel-Dieu at Windsor, during the five-year period, 1937 to 1941, inclusive, there were 220 operations for non-malignant disease of the bile passages. There were 17 deaths in this series, a mortality rate of 7.7%. Of the 220 operations, 180 were on females and 40 on

males, a ratio of 4½ to one. Of the 180 females, 165 had born children, and 15 were nulliparous. If we add the 15 nulliparæ to the male group, it still leaves a ratio of three to one as proof that pregnancy is an important factor in the etiology of gall-bladder disease. Of the 220 operations, 180 were cholecystectomies, 32 were cholecystostomies, 5 were for the removal of the common duct stone in cases in which the gall bladder had previously been removed; one for removal of stone in a long cystic duct, two months after the gall bladder had been removed; and two were for intestinal obstruction by a large gall stone that had ulcerated into the duodenum and caused obstruction in the small intestine. Nine of the 180 patients with cholecystectomies died, a mortality rate of 5%; and of the 40 other operative procedures, mostly done on bad risk patients, who it was considered would not stand the removal of the gall bladder, 8 led to death, a mortality rate of 20%. Of the 220 cases, stones were present in 186, or 84.5%.

Of the 34 cases operated on in which no stones were found, the pathological report showed definite disease present in at least 26, leaving about 8 cases in which there may be some doubt as to the correctness of the diagnosis of gall bladder disease. Of the 180 females operated on, 11 died, a mortality of 6.1%; and of the 40 males, 7 died, a mortality of 17.5%, illustrating the fact that while gall bladder disease is more frequent in women, it is more dangerous in men. The average age of the whole group was 47.4 years, and was approximately the same for male and female. The average age of the fatal cases was 54 years, illustrating the fact that it is the older, and therefore, the longer-standing, cases of gall-bladder disease that carry the greater operative risk. In 24 of the 220 patients, stones were removed from the common duct, three of these patients died, a mortality rate of 12.5%.

Of the seventeen deaths in this series of 220 operations, five patients died of ruptured gall bladder, with peritonitis, and four of uræmia. Two patients died of post-operative cardiac complication and one of pneumonia; two died of hæmorrhage, and there were two so-called "liver deaths", both about 48 hours after operation with extremely high temperature. One patient died following operation for intestinal obstruction by a large gall stone. This represents about an average cross-section of the causes of death, following operations on the biliary tract. Of the 17 deaths, 16 were patients who had definite symptoms of gall-bladder disease for many years, with stones found in the gall bladder, or ducts, or both. No doubt, if they had been operated on in the early stages of the disease, when they first had definite symptoms, the surgical problems would have been much simpler, and the risks almost negligible.

While I would urge most emphatically the importance of operating early in the course of chronic gall-bladder disease, I should like to sound a word of warning against operating for indefinite symptoms. The individual who has "flatulent dyspepsia", but gives no history of attacks of gall-stone colic, or of any attack of pain that might possibly have been an acutely obstructed gall bladder, and gives no history of jaundice, is better carried along on medical treatment. Even though such a patient's gall bladder fails to fill and empty properly in the cholecystograms, or his duodenal drainage shows cholesterol crystals in his "B" bile, I would let him go on belching, without a scar in his abdominal wall, because my experience with operating on that type of cases has been disappointing, both as to the amount of disease found, and the results achieved. Their flatulent dyspepsia will rarely be changed by the removal of the gall bladder, because it is usually due either to over-eating, over-drinking, or to the influence of the mind over the neuromuscular control of the intestinal tract.

Cancer is so commonly regarded as a disease of old age that it is worth while bearing in mind that it can occur in extreme youth and that the various known preventive measures, such as the avoidance of continued irritation of any part of the body, cannot be commenced too early in life. According to official figures, 1,103 children under 15 years of age died from cancer in the United States in 1939, and in the state of Massachusetts the death rate from cancer in childhood was greater than those for whooping cough, measles, diabetes, pulmonary tuberculosis, scarlet fever, and typhoid fever. In the United States during the past 25 years the number of deaths from cancer in children has increased while for many diseases common in infancy and childhood there has been a progressive decrease.—*J. Roy. Inst. of Hyg. & Pub. Health*, 1943, **6**: 59

Case Report

A CASE OF TUBERCULOUS TRANSVERSE MYELITIS

By J. J. Quinlan, M.D.

Staff of Nova Scotia Sanatorium, Kentville, N.S.

The literature contains very few reports of spinal-cord tuberculosis. Even more unusual is a typical localized transverse myelitis of tuberculous causation. We herewith present a case that came under our care recently which provided a very interesting problem in differential diagnosis.

A.B., white, aged 21, Royal Navy, was admitted to the Nova Scotia Sanatorium on July 24, 1941. He gave a history of having developed a pain in the right side of his chest about six weeks previously. His medical officer made a diagnosis of pleurisy and sent him to a military hospital. There, x-ray examination of the chest revealed a bilateral, moderately advanced, pulmonary tuberculosis complicated by a pleural effusion on the right side.

On admission to the Sanatorium his symptoms were loss of weight and strength, evening temperature to 101° F., and an unproductive cough. General physical examination, including the routine, rather thorough, neurological investigation, revealed no abnormalities of note. The physical examination of the chest revealed signs of a pleural effusion at the base of the right lung but no râles were elicited, as one might have expected with the parenchymal lesion present. A complete blood examination, including the Kahn test, was within normal limits. The urine showed no abnormalities. The patient did not have any sputum for examination. A stereoscopic x-ray examination of the chest revealed the presence of a scattered, recent tuberculosis throughout the right lung with a small pleural effusion at the base. There was a similar scattered lesion within the apex of the left lung to the level of the second rib.

His case was discussed at the weekly Staff Conference and it was decided to carry out a period of strict bed-rest treatment. Under this regimen the patient began to improve. He gained weight, the temperature became normal, and his cough disappeared. Satisfactory improvement continued until October, 1941, when he began to complain of pain in the lumbar region and some frequency of urination. The urine was found to contain a moderate amount of albumin and numerous pus cells. A urinary antiseptic was prescribed and the dysuria, nocturia and frequency of micturition promptly disappeared. However, the back pain persisted. X-ray examination of the spine and a complete gastro-intestinal x-ray series revealed no abnormalities of the spine or gastro-intestinal tract.

The back-pain soon began to radiate down the limbs, but a few days later it disappeared completely, leaving only a stiffness and weakness of the leg muscles. This weakness became progressively worse and on November 15, 1941, the patient had lost the use of his lower limbs.

Neurological examination at this time revealed the following findings: Sensation of pain, heat and cold were markedly impaired over the lower limbs, with a definite level at the groin, anterior superior spines and the upper sacral region. Sensation to touch was impaired to a lesser degree. Joint-sense was good. The Babinski test produced a bilateral extensor response; the lower abdominal reflexes were absent; the deep reflexes were increased; and there was good control of the bladder and bowel sphincters. Lumbar puncture revealed the spinal fluid to be under 40 mm. pressure of water and the Queckenstedt test revealed a definite spinal block. The fluid was clear, but contained 100 mg. of protein per 100 ml. and 100 mononuclear cells per c.mm.

On the strength of these findings a spinal cord tumour was suspected. It was decided by our staff surgeon to perform an exploratory laminectomy. However, the evening before the operation it was found that the patient could move his toes again. As this man came under the sponsorship of the Department of Pensions and National Health it was decided to request a medical and surgical consultation from Camp Hill Hospital. This was immediately obtained, and in view of the physical findings plus the recent slight improvement in the condition of the patient the diagnosis was changed tentatively to a transverse myelitis and expectant treatment recommended.

The degree of paralysis continued to lessen

and, within a month, the patient could stand with some assistance. At this point improvement ceased and the condition remained stationary for about six weeks. After this period, complete paraplegia recurred and this showed only very slight improvement again during the next two months.

In June, 1942, bladder and bowel paralysis supervened. A retention catheter was placed in the bladder. In this manner, automatic tidal irrigation of the bladder was carried out.

From this point onward, the course of the disease was progressively downhill, although x-ray examination of the chest revealed that marked improvement had occurred within his lungs. The patient lapsed into coma on September 7, and died three days later. The actual cause of death was a pyelonephritis.

Permission was obtained for a limited autopsy. The spinal cord was removed *in toto*. There was no evidence of tumour. There was a gross caseous lesion beginning two inches above the lumbar enlargement and extending upwards for about one and a half inches. Microscopic examination by the Provincial Pathologist revealed involvement of the nerve roots of the lumbar enlargement by a tuberculous meningitis and areas of caseation were visible in the nerves themselves. Sections through the caseous lesion of the cord revealed typical giant cells and evidence of caseous tuberculosis.

Clinical and Laboratory Notes

COMPLICATIONS OF ANÆSTHESIA

By Surgeon-Lieutenant C. M. Learmonth, R.C.N.V.R.

Montreal

The following experiences with anæsthetics are reported as presenting problems of interest. They occurred during the course of training in anæsthetics which has been arranged for service men in Montreal. The comments are the results of the discussion of the problems with those directing the course.

CASE 1

Male, age 64 years, with lower right quadrant mass, which was to be surgically explored. Preoperative medication was morphine gr. ⅛ and scopolamine gr. 1/200, given hypodermically one and a half hours before operation and repeated again three-quarters of an hour before operation. Using the Etherington-Wilson technique 13 c.c. of 1:1,500 nupercaine (percaine) was given with the patient in the upright position for 45 seconds. Oropharyngeal oxygen therapy and an intravenous injection of normal saline into the right malleolar vein were commenced immediately after. Later, a transfusion of citrated blood was commenced. Within the first fifteen minutes the systolic blood pressure fell from 120 to 40 mm. of mercury and the pulse rate from 100/min. to 80/min. The blood pressure gradually rose to 56 mm. To raise the blood pressure higher neosynephrin 0.5 c.c. was added to the intravenous solution. The systolic pressure rose to 82 mm. of mercury and remained at this level throughout the operation. On account of restlessness the patient was given morphine sulphate, gr. ¼, intravenously. The operation lasted two hours. The patient returned to the ward in fair condition. Fifteen minutes later he lost consciousness, became cyanotic and pulseless. The anæsthetist was called to the ward and found the patient with an obstructed airway. The tongue was pulled forward and the head postured and improvement rapidly followed.

Comment.—Obstruction and therefore anoxia caused by the depression of the patient were due to (*a*) relatively large total dose of morphine in a 65-year old man; (*b*) cessation of surgical stimulation.

Respiratory and circulatory collapse occasionally occur when a patient's position is suddenly changed during or following a long operation. There is usually a considerable respiratory and circulatory depression immediately following an operation. In one group of cases followed by Snyder the cardiac output dropped on an average of 40% and the systolic blood pressure dropped on an average of 20 mm. of mercury.

CASE 2

A husky 40-year old former lacrosse player was operated on for the removal of a bony spike, the sequela of a fractured left rib. Preoperative medication was nembutal gr. iii two hours before operation and morphine sulphate gr. 1/6 and atropine sulphate gr. 1/150 one hour before operation. The patient was anæsthetized in the right lateral position with the kidney rest elevated so as to spread the ribs on the upper left side. Anæsthetic agent and method was cyclopropane with circle absorber. During the operation a small rent was accidentally made in the pleura.

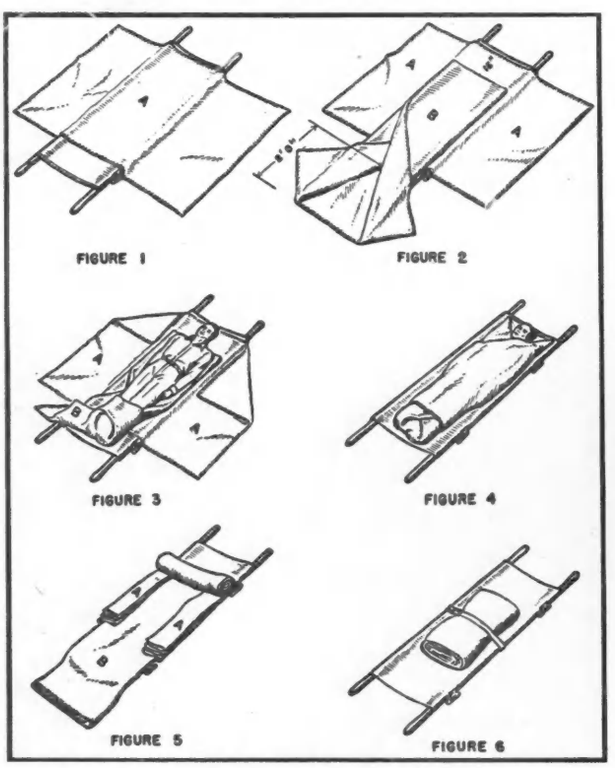
At the close of the operation the patient was returned to the supine position and the anæsthetic mask removed from his face. He gradually became cyanotic. The anæsthetic mask was replaced on the face and the patient was given high oxygen and cyclopropane with immediate improvement of colour. The patient was kept anæsthetized, since it was believed that the accidental pneumothorax was the main cause of the anoxia and aspiration of the air was anticipated. It was noticed at this time that there was also a marked indrawing of the right chest on inspiration, therefore, a tentative diagnosis of atelectasis of the right lung was also made. This was treated by introducing an endotracheal tube and aspirating the trachea with a fine catheter. Coughing ensued and the indrawing of the right chest disappeared. Cyclopropane was now stopped without recurrence of the cyanosis. Air was later withdrawn from the left pleural cavity.

Comment.—Anoxia caused by a combination of (*a*) accidental pneumothorax of the left chest; (*b*) pressure atelectasis of the right chest caused by the kidney rest. The impeded ventilation of the right and left lungs was not noticed until the high oxygen content of the inspired air was changed to the 20% oxygen of the atmosphere. Tracheal aspiration initiated a cough which forced the compressed right lung to expand.

BLANKETING CASUALTIES

(The following circular from the office of Civilian Defence, Washington, D.C., contains information of considerable practical value.)

The British (Wanstead) method of blanketing casualties mentioned in Circular, Medical Series No. 20, U.S. Office of Civilian Defence, is described below. Using two blankets as described, there are four thicknesses beneath the patient and two above. The feet are tucked in snugly and are kept warm by the use of this technique and the head is also protected against the cold. When the blanket fold is completed it securely fixes the extremities and trunk so that it can be used as a blanket carry, if necessary.



PREPARING THE STRETCHER

1. Place blanket A lengthwise across the stretcher with one side close to the head end of the stretcher, and one end of the blanket having a slightly longer overlap of the stretcher than the other end (Fig. 1).

2. Fold blanket B in thirds lengthwise and place over A, the upper edge of this folded blanket being about 15 inches below the upper edge of blanket A (Fig. 2). For very tall persons it is necessary to lay blanket B farther down on the stretcher, to permit its lower end to extend a sufficient length below the patient's feet so that it may be folded up and around them in the manner described below.

3. Open the folds of blanket B for about 2 feet at the foot end (Fig. 2).

WRAPPING A PATIENT

1. Bring the foot of blanket B up over the feet, with a small fold between the feet.

2. Tuck the two open folds of blanket B closely over and around the feet and ankles (Fig. 3).

3. Turn in upper corners of ends of blanket A (Fig. 3), wrap shorter end of blanket A over patient and then the longer end and tuck well in at side (Fig. 4).

BLANKET ASSEMBLY FOR TRANSIT

1. Proceed as under 1 and 2 for preparing a stretcher.

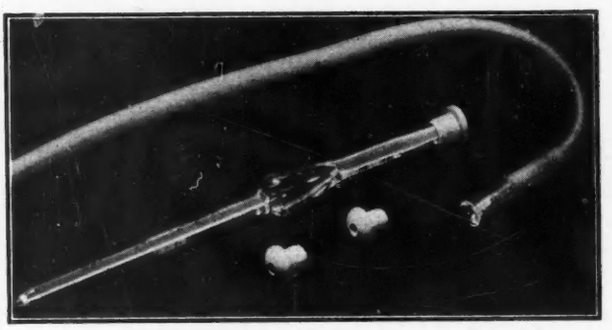
2. Fold in the two ends of blanket A in accordion pleats (Fig. 5); fold in the foot end of blanket B; then roll the blanket and make secure (Fig. 6). A hot-water bottle may be placed in the centre of the blanket pack to keep it warm.

A USEFUL STOPPER FOR BLOOD PIPETTES

By W. R. Caven, M.A., M.B.

Toronto

One of the minor problems in medical practice has been the transportation of diluted blood in a pipette from the patient to the laboratory. Various devices are on the market for use in sealing the pipette but most of these depend on



the use of a spring clip which is cumbersome and will usually not fit in the hæmocytometer case. The illustration shows a simple method of overcoming the difficulty. The small rubber cap that is used to fit over the upper end of the pipette after removal of the rubber tubing is a stopper from a bottle of concentrated liver extract supplied by the Connaught Laboratories. To put it in place a finger is held over the point of the pipette, then the tubing is detached and the stopper pushed on. The pipette can then be replaced in its usual groove in the hæmocytometer case without danger of leakage.

Editorial

THE MEDICO-LEGAL ASPECT OF TRICHINIASIS

THAT trichiniasis occurs in Canada from time to time is quite well known. Apparently, however, it has only recently been the ground for litigation. This took the form of an action against a meat pedlar and a packing company by a woman who alleged that she developed trichinosis from eating pork sausages sold by the defendants.*

The facts were that the sausages were cooked in the frying pan in the usual way, but the woman seems to have eaten some of them soon after the cooking began, as did her two children who also developed trichinosis. Her husband, on the other hand, who did not develop the disease, came in much later, when the sausages were more completely cooked.

The evidence on the whole then supported the contention that these sausages were the source of the infection. Was there any liability to the consumer on the part of those producing the meat? First of all, a packer is not to be considered as a "manufacturer" of the meat he sells. He does not manufacture the hogs and can have nothing to do with their being infected with trichinæ. The pork in question had been regularly inspected by Government officials and stamped as "approved", but it was freely admitted that such inspection made no pretence at detecting the presence of trichinæ. No tests for these are commercially feasible, since the only methods by which the encysted form of the parasite can be detected require either artificial digestion of the hog muscle, or microscopic sectioning. Obviously, neither of these can be extended to cover the whole carcass, and a partial examination would only give a sense of false security.

The packer therefore could not know whether his pork contained trichinæ, or not, and there was no government regulation requiring that he should, so that he could not be called negligent regarding its condition in this respect nor could he have warned the plaintiff, even if such warning were called for.

The question then arose as to whether there might be liability under the Animal Contagious Diseases Act, which forbids the sale of meat from an animal infected with any infectious or contagious disease. Here too it was argued that since the packer was unable to find out whether his pork contained trichinæ, it would be extremely harsh legislation if strictly applied in these circumstances, and indeed would prohibit the sale of fresh pork at all.

Further consideration also made it clear that a hog with encysted trichinæ was not an unhealthy or diseased animal, since the parasites had become innocuous so far as that animal was concerned. Finally, there is the telling point that no trichina-infested meat need be unfit for eating, if it is properly cooked, since the trichinæ are destroyed by heating to 131° F.

In view of these arguments the action was dismissed with costs.

This case is of great interest as being the first of its kind in Canada. Recently a great deal of publicity has been given to the high incidence of this parasite in man in the United States. In this country the incidence is low—about one-eighth of the American figure. This is almost certainly due to the Canadian law which compels the cooking of all garbage fed to pigs. It is improbable too that trichiniasis will increase. Depending as it does for its continuance on feeding raw pork scraps to pigs, the meat shortage should tend to make it decrease instead of increase. However, a certain amount always exists and it should be realized not only that it cannot be detected by inspection, but that no attempt is made to do so. The onus of prevention is on the public. Complete protection is obtained by very easily applied methods in cooking.

* The case of Yachetti *et al.* v. John Duff & Sons Ltd. and Paolini; tried at Hamilton, Ont., October 2 to 7, 1942, without jury.

Editorial Comments

The Dieppe Wounded

A review of the casualties amongst Canadians at the Battle of Dieppe has been published by Colonel J. A. MacFarlane.* The peculiar difficulties in handling the wounded in this action are made clear. The number of casualties could easily have been very much higher than even our admittedly heavy losses, and the evacuation of those that were saved reflects the very highest credit on the battalion medical officers and the naval units.

Colonel MacFarlane's review covers both the early and late treatment of the wounded. Sulfonamides were used as early as possible, beginning during the voyage home. Not more than 30% of the cases received them before admission to hospital. In all the hospitals oral administration was begun on admission and in 92% of cases some type of sulfonamide was used at the time of operation. It is noteworthy that no case of clinical tetanus developed in the whole series of 600 men, which is to be attributed to the general immunization with tetanus toxoid. Antitoxic serum was given however in 6% of these cases. Apparently the procedure as to whether a boosting dose only should be regularly given has not been standardized.

Resuscitation, including transfusion with blood or blood substitutes was carried out in about 10% of cases. It was found possible, and was certainly regarded as most valuable, to give transfusions with dried serum, even on board a small boat which was being subjected to heavy enemy attack.

With respect to the types of wounds comment is made that in wounds of the chest conservative treatment gave reasonably encouraging results. Repeated aspiration was regarded as valuable. The greatest stress is laid on the value of the active co-operation of medical specialists in this group, a point which incidentally is similarly emphasized in histories of base hospitals concerning the same kind of wounds in the last war.

In abdominal wounds the mortality was directly related to the delay in reaching the surgeon. In dealing with wounds of the extremities the value of the principles laid down by Trueta was fully confirmed; that is, wide exploration and debridement; packing; immobilization; and infrequent dressings.

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* *The Lancet*, April 17, 1943, p. 498.

Medical Economics

MEDICAL SERVICES IN SOUTH AFRICA

The situation of the medical profession in South Africa at the moment is of peculiar interest to us. The Government there has appointed a National Health Service Commission in response to public demand for improvements in health measures and the medical profession of the country is in process of preparing its views as to how this may best be done. In many respects the same problems as ours are being faced.

An editorial in the *South African Medical Journal*, December 26, 1942, begins by saying: "In the present instance our efforts are definitely in the first instance aimed at providing better health conditions for the community as a whole. We take it for granted that any health services that may be set up cannot function properly unless the conditions under which those operating it—the medical and allied professions — are satisfactory. Naturally, therefore, in any such scheme we must look after our own interests, but that is not our first aim," and later: "If the Association can now speak with a united voice, there is a reasonable prospect of our views being seriously considered and given effect to."

The profession is being given the opportunity of presenting its views to the Government Commission, and is trying by means of a questionnaire (just as was done in Canada) to assemble opinion. It is realized that whatever scheme is recommended, or even adopted, "is unlikely to remain unmodified. Experience is sure to show up weaknesses and to require modifications". It is felt that the main thing is to get into operation some scheme which has the general support of the profession.

Incidentally, the South African Medical Association up to 1941 had placed itself on record as being pledged to support a National Health Insurance Scheme if introduced by the Government. It became evident however that this position was not supported by the majority of the Association's members, and a referendum later on reversed the original decision of supporting a Health Insurance scheme, thus leaving the Association free to support any policy it thought fit.

A Planning Committee now has the task of gathering opinions and evolving some scheme which will receive general support. There is not enough material yet to hand for any definite outline, but evidently the same problems are being dealt with as we have before us. There seems to be a feeling that some form of Health Insurance will have to be instituted, even though the experience of other countries in this matter has not been completely satisfactory for either side. The position of benefit society practice is

evidently of much greater significance than with us.

The question of "socialized medicine" (corresponding to state medicine apparently) is being faced very frankly. The questionnaire includes questions as to views on this, although the editorial opinion seems to reflect a definite body of feeling against any health scheme which would give medical practitioners the status of civil servants.

There seems to be a fair amount of agreement on the point that any scheme adopted should be administered by a commission mainly composed of medical representatives.

We have no details yet of any further developments in South Africa, but will refer to the subject again as opportunity occurs. H.E.M.

IMPLICATIONS OF HEALTH INSURANCE BASED ON ACTUAL EXPERIENCE

By J. A. Hannah, M.D.

Managing Director, Associated Medical Services Inc., Toronto

The imminence of Health Insurance is indicative of the need for everyone to acquaint himself with all available facts in regard to it. Lack of such knowledge may place everyone in the hands of a bureaucratic political machine which will be neither satisfactory nor efficient in its operation. With these facts in mind, Associated Medical Services intends to present a series of short terse articles based on experience. It is not our intention to do more than state facts as indicated through our experience. From these facts each can draw his conclusions. In the midst of hastily prepared "estimates" based on theory, sound facts based on experience may save everyone a good deal of difficulty and embarrassment.

Government assistance will be essential to make the service available to the very low income group and the indigent. Its successful operation will, however, depend upon retaining responsibility for the expenditure of finances close to the source of consumption. Expenditures made from a common fund controlled far from its source under government auspices tend to destroy that sense of personal responsibility so essential for successful operation.

Associated Medical Services, a non-profit organization for budgeting the cost of medical care is in its sixth year of successful operation. A recent analysis shows that 74% of the first 1,000 numbers given to family groups (representing 1,880 individuals) are still subscribing. The remaining 26% includes cancellations from all sources, including enlistments and deaths. In view of the fact that over 85% of subscriptions are paid monthly, this record is outstanding.

Out of this experience Associated Medical Services presents for your consideration the facts herein contained. We will be pleased to assist in any way possible in helping all to understand the implications of providing a sound and economical Medical Service.

COSTS

On the basis of free choice of doctor paid on a fee for service basis, costs appear as follows:

Doctors' fees							
Between	$1.06	and	$1.08	per	month	per	subscriber
Hospitalization							
Between	0.37	"	0.40	"	"	"	"
Nursing							
Between	0.06	"	0.08	"	"	"	"
Total medical costs							
Between	1.49	"	1.56	"	"	"	"
Reserve							
Between	0.18	"	0.20	"	"	"	"
Administration							
Between	0.18	"	0.20	"	"	"	"

Administrative costs could be considerably reduced if subscribers and subscriptions were secured by group methods.

Medical costs per person can also be materially reduced if and when the profession is paid for the low income and indigent groups as will be the case under any government plan. The problem of how much such costs might be reduced will form the basis of a later article.

In a family of husband and wife, the husband requires on the average 22% of the service rendered and the wife 78%. In a family with husband, wife and two children, the husband will get on the average 10% of the service and the wife and children 90%.

A partial plan, either in regard to (1) Services or (2) Family, fails both in regard to employer and employee, and the doctor.

1. If hospitalization alone is covered, the employee is left with at least 75% of his expense which, in a serious illness, is still sufficient to dissipate the life-savings of the average workman (if he has any), or what is more usual, to mortgage his earning capacity for years to come.
2. If the family of the employee is not protected it leaves the married employees' responsibility unprotected to the extent of from 78 to 90%.

In either (1) or (2) the objects of such a plan are defeated in that it leaves the employee with an unmanageable responsibility in relation to his income. This in turn defeats the objects of the employer, leaving him with a dissatisfied and inefficient employee. It defeats the purposes of the physician in that it leaves him with a continuing unfair load in regard to the inability to collect a reasonable sum for the services which he must render.

To be successful the administration of any such plan must be not only fair but fearless and have very definite checks and controls over the services demanded and rendered. It must be entirely free of pressure from either politics,

employers, or employees. All matters of adjustment must be left entirely in the hands of the administration. The only appeal allowed must be by the beneficiary through the regular channels to the ordinary courts, with which there must never be any interference.

We commend to consideration two articles: (1) "Implications of Health Insurance", *Drug Merchandizing*, February 15, 1943, p, 97. (2) "Some Problems Facing Industry and the Medical Profession in Relation to Health Insurance", *Industrial Canada*, March, 1943, p. 68.

Men and Books

WILLIAM SMELLIE*

Master of British Midwifery

By Ross Mitchell, M.D.

Winnipeg

In these days, when obstetrics is a science as well as an art, it is difficult to envisage midwifery as it was practised in the first half of the eighteenth century. Then deliveries were almost invariably conducted by female midwives, most of whom were of the Sairey Gamp type. Medical men, for the most part, scorned to practise midwifery, and as the few cases in which they were called in by the midwives to render assistance were almost invariably difficult, dangerous and abnormal, they had few opportunities to master the art of safe delivery. The obstetrical forceps was only beginning to come into use, but destructive instruments such as the crochet and the blunt hook were frequently employed. The blessed gift of anæsthesia was not to be granted to mortals for nearly a century, and the pangs of a woman in travail were a synonym for the utmost in suffering. Epidemics of puerperal fever were common, and death from childbirth was a leading cause in the bills of mortality.

It is true that there had been notable figures in the field of obstetrics prior to 1750. Soranus of Ephesus who practised in Rome in the second century A.D., had a unique knowledge of female anatomy and his four books on diseases of women influenced obstetrical thought and practice for 1,200 years. Vesalius in the sixteenth century laid the foundations of modern anatomy; Ambroise Paré (1510-1590) revived the practice of podalic version; William Harvey (1578-1657) wrote on embryology and labour in human beings; François Mauriceau (1637-1709) in his "Traité des Maladies des Femmes Grosses", described the technique of delivery in breech presentations, the management of the placenta, tubal pregnancy, and difficult labour from involvement of the cord. Hendrick van Deventer (1651-1724), who lived at The Hague, was the first to distinguish between the flat and the generally contracted pelvis, and gave the first accurate description of the pelvis and its deformities, with the effect of the latter on labour. Louise Bourgeois (1563-1636) delivered Marie de' Medici, the wife of King Henri IV of France, in her six confinements, induced premature labour in women with contracted pelves and wrote an account of the birth of the princes and princesses of France. Justine Siegemundin, the most celebrated of the German midwives, was made Court Midwife by order of King Frederick III of Prussia (1690), and published a record of instructive cases for the use of midwives.

The return of the male obstetrician to the confinement chamber, after an absence of thirteen centuries received royal sanction when Le Sieur Boucher was called by Louis XIV to attend Mlle. de la Vallière, his mistress. The king is rumored to have been an interested spectator of the proceedings from the concealment offered by some curtains.

In 1670 Julien Clément, then only twenty-one years old, attended Madame de Montespan, mistress of Louis XIV, at the birth of the Duc de Maine, and in 1682 he delivered the Duc de Bourgogne, eldest child of the Dauphin and the Dauphine, Marie Anne de Bavière. Clément received the title of "accoucheur" for his troubles, as the name of man-midwife was considered too undignified for one of his standing, and he was afterwards called to Spain on three occasions to attend the wife of Philip V. Peter Chamberlin, of forceps fame, attended Queen Henrietta Maria, wife of Charles I, during a miscarriage in 1628, and in 1688 his son, Hugh, delivered the wife of James II of a son who became "The Old Pretender", and in 1692 he attended the future Queen Anne at the birth of a son who immediately died. William Hunter was in attendance at the birth of King George IV, though George III's Queen was actually delivered by Mrs. Draper. Obstetricians have reason to be grateful to royal courts for setting the fashion of male accoucheurs.

The acceptance of the obstetrical forceps in the first half of the eighteenth century as a means of delivery in difficult cases further aided the change, since the men had a better knowledge of anatomy and were willing to accept greater responsibilities. Sir Richard Manningham (1690-1759) established the first British lying-in wards in 1739 and John Leake (1729-1792) founded the New Westminster Lying-in Hospital in 1767. John Maubray in 1724 recognized the importance of prenatal care. He gave it as one of the duties of the man-midwife to watch the patient during pregnancy so as to prevent all "preternatural disasters", and throughout the eighteenth century particular

* Read at the Seventy-third Annual Meeting of the Canadian Medical Association, Section of Historical Medicine, Jasper Park, Alta., June 18, 1942.

attention was paid to diet, hygiene and the evacuations of the patient.

It was upon such a scene that William Smellie came. He was born at Lanark in 1697. In all probability he was an only child and he received his education at the Grammar School in Lanark. He never lost his affection for the district and the school, for quite early in his career he acquired a small property there, and in his will he directed that:

> "I, Dr. William Smellie, for the regard that I have for the School of Lanark, bequeath to the same all my Books, mapps, and pamphlets, except those of Medicine, Surgery and Pharmacy, for to begin a Liberary there. Also I bequeath Two Hundred Pounds Sterling for repering the School House according to a Plan I have left.
>
> (Sgd.) William Smellie."

He also bequeathed to the school "9 English Floots with the thick quarto gilt Musick Book". In addition to his taste for music he loved painting. The only portrait of him was painted by himself; the original is in the Royal College of Surgeons, Edinburgh, and a print is in the library of the Royal Society of Medicine, London.

The only way of entering the profession at that time was by serving an apprenticeship with a medical practitioner. Smellie probably studied with Dr. John Gordon, a well-known practitioner in Glasgow, with whom Tobias Smollett also later served his apprenticeship. This would account for the friendship between Smellie and Smollett. The latter aided Smellie in the preparation of his Treatise of Midwifery.

In 1720, being then twenty-three years of age, Smellie began practice in Lanark, and, although so poor that he was obliged to sell cloth to keep himself in daily bread, he yet made careful notes of his cases. In 1733 he was admitted to the membership of the Faculty of Physicians and Surgeons in Glasgow as a surgeon. In 1745 the University of Glasgow conferred on him the degree of M.D. For about nineteen years he carried on a large general practice from Lanark, then a town of about 2,000 inhabitants. His bias toward obstetric practice was manifest from the start. Early in his career he gained the friendship of William Cullen, an exceptionally able physician of Hamilton, who later became Professor of Medicine in Glasgow University and four years later Professor of Medicine and Chemistry in Edinburgh. Cullen was also the friend and teacher and partner for a time of William Hunter.

Like so many other Scots, Smellie felt the lure of London, and in 1739 he went there to gain a greater knowledge of obstetrics. The teaching of obstetrics in London was in a chaotic state, so he studied in Paris under Gregoire. However, he formed no exalted opinion of French teaching, and soon returned to London, settling in Pall Mall. It was to Smellie's house that William Hunter came on leaving Hamilton in 1741. In that year Smellie began the teaching of obstetrics. Immediate success crowned his efforts, though he began with almost no capital. It was charged by his enemies that he advertised his lectures on a street lamp, and he did not deny that poverty had compelled him to resort to such a device.

There were good reasons for his success as a teacher. He taught midwifery clinically and in the presence of his pupils he delivered 1,050 women during his first ten years of teaching. Further to assist his teaching he used a "machine" or obstetric phantom, designed by himself. A leader of the irate female midwives, Mrs. Elizabeth Nihell, or Nikell, of Haymarket, referred scathingly in 1760 in her "Treatise on the Art of Midwifery" to Smellie's dummy: "This was a wooden statue, representing a woman with child, whose belly was of leather, in which a bladder full, perhaps of small beer, represented the uterus. This bladder was stopped with a cork, to which was fastened a string of packthread, to tap it occasionally, and demonstrate in a palpable manner the flowing of the red-coloured waters. In short, in the middle of the bladder was a wax doll, to which was given various positions. By this admirably ingenious piece of machinery were formed and started up an innumerable and formidable swarm of midwives." It was Mrs. Nihell who dubbed her rival as a "great horse godmother of a he-midwife".

Smellie's practical mind and mechanical bent inclined him to seek to understand the mechanics of labour. It was the knowledge acquired by diligent observation that enabled him to become such a remarkable practitioner and teacher. He gave us a simple method of estimating the diagonal conjugate diameter of the pelvis, a method which is still practised. In breech delivery he elaborated the method practised by Mauriceau, which is known by their joint names and is in everyday use, and he advocated in difficult cases the application of forceps to the aftercoming head. In diagnosing the position of the presenting head he taught his students to feel for the ear. He showed that, contrary to the view held at that day, the greatest diameter of the pelvis at the brim was the transverse, and not the antero-posterior.

Few men have equalled Smellie in the skilful use of forceps. He became acquainted with Dusé's forceps through Butler's Edinburgh Medical Essays (1735), but found them too long and ill-contrived. Characteristically, he set about to improve them. If he did not invent the so-called English lock, he made it standard for British forceps. His short forceps proved the most efficient instrument of the time. Coincidently with Levret of Paris he added the pelvic curve. For use in mid and high positions he designed the long forceps. For all this, he was restrained in his use of the forceps, for he states that only 10 out of 1,050 labours required instrumental delivery. In writing to his old

master, Dr. Gordon, he says, "I have laid it down as a maxim to myself, and to the gentlemen who attend my course, never to use any instrument or violence, but where it is absolutely necessary for the safety of the mother and child". The forceps was not the only instrument he improved, for to him must be accredited the perforating scissors that bear his name, also the curved and double-articulated crochet. He was the first obstetric writer to lay down safe rules for the application of forceps, and his rules, formulated in 1751, are practically those that obtain today.

Smellie's treatment of persistent occiput posterior is worthy of mention. He not only used manual rotation for this condition but also the forceps. The value of his straight forceps in this connection is obvious.

He was well acquainted with accidental hæmorrhage and placenta prævia, and he also paid especial attention under this head to diet, air, sleep, rest, excretion and the "passions of the mind". For laceration of the perineum he recommended immediate surgical repair.

The fruits of thirty-one years of practice and ten years of teaching were presented to the obstetrical world in his "Treatise on the Theory and Practice of Midwifery" published at London in 1751. The work gained an immediate popularity, for in 1765 the sixth edition was published in Dublin. It was translated into several languages. He was fortunate in obtaining the assistance of his friend Tobias Smollett in its preparation, a circumstance which may account for the literary quality of its composition.

In 1753 he published "A Set of Anatomical Tables". We are told that twenty-six of these were engraved from drawings done by Mr. Ramsdyke and that in eleven others the author was assisted by Camper, Professor of Anatomy and Botany at Amsterdam. The plates show the pelvis, the external genitalia, the pregnant uterus at various months with its contents, twins, the process of normal labour with illustrations of various positions of the head, the application of the forceps in head and face delivery, the head impacted in the pelvis, with overlapping cranial bones, breech presentations, the application of forceps to the after-coming head, the head left *in utero,* and instruments with their mode of application. These plates are superior to any that had hitherto appeared, and Michaelis, the classical writer on the contracted pelvis, says, "they have perhaps achieved more in the spread of correct ideas of labour than all the books which have ever been written on the subject".

Though Smellie's "Treatise on Midwifery" had a large sale, this was not true of the "Set of Anatomical Tables". Dr. James Hamilton, Junior, in 1796, said of this atlas: "Within these few years the copperplates of Dr. Smellie's work (the first publication in this island calculated to explain the mechanism of human parturition) from which no more than eighty copies had been thrown off, were actually purchased for the price of old copper."

In the preface of his "Treatise on Midwifery" Smellie stated that in his ten years of teaching he had given upwards of two hundred and eighty courses of midwifery, for the instruction of more than nine hundred pupils, exclusive of female students. Among his pupils were Denman, William Hunter, Dr. McBride, of Dublin, and Professor Roederer, of Gottingen.

His unremitting diligence in practice and teaching undermined Smellie's health, and about 1759 he retired from active work and returned to Lanark. There he purchased additional land on the outskirts of the town, which with his former holding constituted his small estate of Smellom. He busied himself in completing the third volume of his Treatise. The manuscript was transmitted to Smollett and even delivered to the printer when Smellie died. On the flyleaf of William Hunter's copy of Smellie's Treatise there is the following note in Hunter's handwriting: "The author died of an Asthma and Lethargy at his House by Lanark in Scotland in March 1763. He was buried close to the wall of St. Kenigern's Kirk in Lanark."

About the time of Smellie's departure from London there was a disturbance of his friendship with William Hunter, who had once been master and pupil. Smellie referred to it in two notes, one to Dr. Clephane, the other to Dr. William Pitcairn, President of the Royal College of Surgeons. Before Smellie went off to Scotland Dr. Hunter heard that he complained of him, and Dr. Hunter knowing that it was without reason, wrote to him to beg and insist upon a meeting at the British Coffee House with their common friends, Dr. Clephane and Pitcairn. This was the occasion of the letter, for Smellie went away without giving that satisfaction. In the letter to Dr. Clephane Smellie remarks "This way I thought safer, after retiring to the gloomy regions, than to have mett in the British C.H. Dr. H's glib tongue." Smellie exhibited discretion in avoiding a crossing of swords with dapper little William Hunter. The latter, with his brilliant intellect and wonderful gift of expression, would have triumphed over his unsophisticated adversary. Nothing has been found in Hunter's publications to justify Smellie's suspicion, and the cause of the estrangement remains obscure.

The character of William Smellie may be learned from a study of his life, from the preface of his Treatise and from his own self-analysis in the letters to Dr. Pitcairn. From these he emerges as a man who, without the external advantages of birth and fortune, yet endowed with industry, diligence and singleness of purpose, and rich in common sense, raised himself to a foremost position in his chosen field. Fasbender, in his "Geschichte der Geburtshülfe" called him "one of the most important obstetricians of

all times and countries". With all his success he was modest, kindly, quick to recognize merit in others, and seized with a high idea of the dignity of his profession. At a time when the nurses were vehemently maligning him, he besought the accoucheurs in their dealings with nurses, *i.e.*, midwives, "to make allowance for the weakness of sex, and rectify what is amiss, without exposing her mistakes. This conduct will effectually conduce to the welfare of the patient, and operate as a silent rebuke upon the conviction of the midwife, who finding herself treated so tenderly, will be more apt to call for necessary assistance on future occasions, and to consider the accoucheur as a man of honour and a real friend."

Although he was ridiculed and maligned not only by the midwives but by some members of his own profession, he did not engage in controversy. He was kindly to the poor women with whom his practice at first lay. In his Treatise he wrote that the 1,050 poor women whom he had delivered in the presence of those who attended him were supported during their lying-in by the stated collections from his pupils. Out of these ministrations there awakened in the minds of lay members of the community a sense of the value of this work, with the result that the chief obstetric charities in London came into existence. Even if this had been his only contribution to the welfare of his community, he would have been entitled to the gratitude of the citizens of London, but his additions to the science of obstetrics make him the benefactor not only of a city but of the whole human race.

CATECHISM IN MEDICAL HISTORY

By Heber C. Jamieson, M.B., F.R.C.P.(C)

Edmonton

QUESTIONS

1. What mistake did Laennec make in his interpretation of the heart sounds which precipitated a fifty year controversy?
2. What English poet and physician described arteriosclerosis in verse?
3. What constituted the Iatromathematical and the Iatrochemical theories of the human organism of the seventeenth century?
4. What Quaker physician was one of the master minds of the nineteenth century?
5. What man noted as a surgeon, physician, sailor, explorer, naturalist and scholar was the first doctor to visit the Canadian North West and leave his name on animals and plants of that region?

ANSWERS

1. He stated that the first sound of the heart was caused by contraction of the auricles.
2. John Armstrong (1709-1799) in the "Art of Preserving Health".

> There is a point
> By Nature fix'd, whence life must downwards tend.
> For still the beating tide consolidates
> The stubborn vessels, more reluctant still
> To the weak throbs of th' ill-supported heart.
> This languishing; these strengthening by degrees
> To hard unyielding unelastic bone,
> Thro' tedious channels the congealing flood
> Crawls lazily, and hardly wanders on;
> It loiters still: And now it stirs no more.
> This is the period few attain; the death
> Of Nature: thus (so heav'n ordain'd it) life
> Destroys itself;

3. The Iatromathematicians believed that all the functions of the body were motivated by physics. The protagonists of this system were Descartes, Borelli, and Sanctorius. The Iatrochemists attributed all vital phenomena to chemical action. V. Helmont, Sylvius, and Willis represented this school.
4. Thomas Young (1773-1829). He was equally at home in the classics, in physics, mathematics, philology, music, and actuarial science. He was the author of the wave-theory of light. The modern concepts of energy, the theory of capillary action, the first decription of astigmatism, responsibility for adoption of the imperial gallon, longitude, and laws of life insurance were a few of his contributions.
5. Sir John Richardson. In 1819 he visited Fort Edmonton while surgeon to the Franklin Expedition to the Arctic. The Richardson ground squirrel, the Richardson kangaroo rat, the Richardson grouse, the Richardson water shrew, the Richardson owl are some of the animals he named. Many plants, including Richardson's grass, bear his name.

Association Notes

Proposed Revisions of the By-laws

The following proposed revisions of the By-laws will be brought to the attention of General Council at its meeting in the Mount Royal Hotel on June 14 and 15, 1943:—

A—*Chapter VIII, Section 4, paragraph 2*

The President, the President-Elect, the Chairman of the General Council, the Honorary-Treasurer, the General Secretary, the Editor and the Managing Editor shall be members ex-officio of the Executive Committee, but only the elective officers shall have the right to vote.

It is proposed that this section be revised to read:

The President, the President-Elect, the immediate Past-President, the Chairman of General Council, etc.

B—*Chapter VII, Duties of Officers*

It is proposed that, after Section 2, a new Section be inserted to read as follows:

Section 3—Duties of the Immediate Past-President

He shall be a member ex-officio of the Executive Committee for the year immediately succeeding the termination of his Presidency.

Renumber the succeeding paragraphs, starting with *Section 4, Duties of Chairman of General Council.* Add to the end of *Section 1—Duties of the President*, the following sentence:

He shall be a member *ex-officio* of the Executive Committee for the year immediately succeeding his Presidency.

C—*Chapter VI, Section 2, Paragraph 4(2)*

Each Division's official nomination of one alternate who will act in the absence by reason of death or illness or from cause acceptable to the President, of the member or one of the members representing that Division.

It is proposed that, after the word "members" in the fourth line, the following words be inserted: "of the Executive Committee".

Medical Societies

La société médicale des hôpitaux universitaires de Québec

Une séance de la Société Médicale des Hôpitaux Universitaires de Québec, etait tenue a l'Hôpital Laval, vendredi, le 2 avril 1943. Suivent les résumés des travaux présentés à cette occasion.

RHUMATISME D'ORIGINE TUBERCULEUSE PROBABLE.—R. Desmeules et P. Richard.

Les auteurs font l'exposé des données de laboratoire sur lesquelles Poncet et ses partisans édifient le diagnostic du rhumatisme tuberculeux dit primitif.

Comme les preuves bactériologiques et anatomo-pathologiques ne peuvent généralement pas être obtenues dans les formes chroniques, ils trouvent plus pratique d'établir le diagnostic sur une impression clinique.

Ils présentent une observation où après avoir procédé systématiquement à l'élimination des causes infectieuses et diathésiques du rhumatisme, ils concluent à l'étiologie tuberculeuse des algies chez un tuberculeux pulmonaire porteur d'une otite bacillaire. Ils citent les statistiques de Dumarest où le rhumatisme n'est qu'exceptionnellement rencontré chez les tuberculeux pulmonaires avec élection marquée pour ceux dont le type anatomo-clinique épouse la modalité fibreuse discrète.

CANCER DES FOSSES NASALES.—G. Léo Côté.

L'épithélioma est, parmi les formes des tumeurs malignes des fosses nasales, celui le plus fréquemment rencontré. A côté de l'épithélioma épidermoide proprement dit, baso ou spino-cellulaire, de l'épithélioma cylindrique, on rencontre assez fréquemment la "Tumeur de Smincke" qui est un lympho-épithéliome, et plus rarement l'adéno-carcinome développé aux dépens de la membrane de Schneider. Chaque forme histologique semble correspondre à un type clinique différent. Quelques considérations sont émises sur le siège, l'évolution et les caractères histologiques de ces différentes formes d'épithélioma. Suit une observation personnelle d'un cancer des fosses nasales survenu chez une fillette de quatre ans.

PÉRICARDITE TUBERCULEUSE.—R. Desmeules.

L'auteur rappelle l'opinion de certains médecins qui affirment que la péricardite tuberculeuse existe chez 4% à 6% des sujets tuberculeux examinés à la salle d'autopsie. Il souligne qu'à l'Hôpital Laval on n'a rencontré la péricardite tuberculeuse que chez 1.3% des bacillaires autopsiés.

Deux observations illustrent la communication. La première observation est celle d'un enfant de cinq ans qui présente de l'érythème noueux suivi de tuberculose ganglio-pulmonaire. Des douleurs précordiales, accompagnées de frottements péricardiques, de fièvre et d'agrandissement de l'ombre cardiaque, font porter le diagnostic de péricardite tuberculeuse. Le malade guérit cliniquement de la tuberculose ganglio-pulmonaire et péricardique.

La deuxième observation concerne un homme de 30 ans. Il s'agit d'un tuberculeux pulmonaire qui souffre de très fortes douleurs précordiales. Les douleurs s'accompagnent de fièvre, de tachycardie, de frottements péricardiques, d'augmentation très marquée de l'ombre cardiaque. L'électrocardiogramme indique un flutter auriculaire.

L'auteur souligne les faits qui permettent de porter le diagnostic de péricardite tuberculeuse: évolution des symptômes péricardiques dans le cadre d'un ou de plusieurs foyers tuberculeux siégeant en dehors du péricarde; frottements péricardiques; agrandissement de l'ombre cardiaque et modification des accidents électrocardiographiques R S et T. La ponction du péricarde demeure le moyen qui permet d'établir un diagnostic de certitude. Elle ne doit être faite que si le diagnostic étiologique est très hésitant, ou encore s'il existe des signes d'épanchement considérable.

MALADIE DE HODGKIN À SYMPTOMATOLOGIE FRUSTE.—L. Rousseau et M. Giroux.

Présentation de deux observations où la maladie de Hodgkin pouvait être facilement confondue avec une tuberculose et avec un état infectieux.

La première observation se rapporte à une jeune fille de 18 ans, présentant une masse ganglionnaire cervicale qui fut confondue avec un ganglion tuberculeux. Après plusieurs mois, une biopsie a montré qu'il s'agissait d'une maladie de Hodgkin. L'évolution de cette affection s'est faite sans fièvre, sans altération importante de l'état général.

La deuxième observation correspond à une maladie de Hodgkin localisée à la rate, sans aucune participation ganglionnaire. Le malade succomba après cinq mois de maladie présentant un syndrôme infectieux. Le diagnostic de maladie de Hodgkin ne fut établi qu'après examen histo-pathologique de la rate.

Séance tenue à l'Hôpital Laval, Québec, le 16 avril 1943.

AMIANTOSE INCIPIENTE CHEZ DES TUBERCULEUX PULMONAIRES.—R. Desmeules, L. Rousseau et P. Richard.

Les auteurs donnent un aperçu histologique de l'amiantose pulmonaire et discutent la valeur des signes cliniques et radiologiques, à la phase incipiente. Ils concluent à la nécessité de faire reposer la preuve de l'amiantose sur le corps d'amiante expectoré. Ils le considèrent comme la signature d'une réaction histo-pathologique pulmonaire secondaire à l'inhalation de poussières d'amiante.

Ils appuient ces considérations par trois observations d'amianto-tuberculose où l'amiantose incipiente, masquée par le tableau de la tuberculose, trouve ses critères cliniques et bio-chimiques dans les commémoratifs d'une exposition aux poussières amiantiques coincidant avec la présence de corps d'amiante dans les expectorations. (Présenté auparavant à une séance tenue à l'hôpital Laval, le 20 novembre, 1942.)

NÉPHROSE LIPOIDIQUE CHEZ UNE FILLETTE DE QUATRE ANS.—M. Langlois et R. Thibaudeau.

L'observation présentée est celle d'une malade où tous les signes cliniques ont orienté vers un diagnostic de néphrose lipoïdique. A cause de l'absence de certain contrôle chimique, absence motivée, l'observa-

tion prêtait à discussion, et c'est dans ce but qu'elle a été présentée.

La présentation de l'observation est suivie d'un court exposé des signes primordiaux de la néphrose lipoïdique.

HYSTERO-SALPINGOGRAPHIE. — F. Gagnon et L. Cayer.

L'exploration radiologique de l'appareil génital de la femme, utérus et trompes, est l'une des dernières applications de la méthode générale de diagnostic par le lipiodol. Les premières recherches furent faites simultanément en France et en Amérique.

La technique de l'opération est très simple, et ne nécessite ni préparation, ni anesthésie, ni soins consécutifs.

Toutefois, cette méthode d'examen exige une instrumentation un peu spéciale permettant une oblitération parfaite de la cavité cervicale, afin d'ampêcher le reflux, dans le vagin, du liquide infecté. La substance employée est un lipïodol pur, légèrement tiédi auparavant, et son injection se fait sous écran pour que l'opérateur puisse suivre le mode de remplissage de la cavité utérine et des trompes et apprécier la quantité de liquide nécessaire: cette dernière varie entre 6 et 20 c.c. Une radiographie est ensuite pratiquée.

Les renseignements tirés sont les suivants:

1. L'état de contractilité de la musculature utérine;
2. l'état de la cavité utérine, *i.e.* son siège, sa forme, son volume, et par voie de conséquence, la présence de corps étrangers, de tumeurs, etc, etc;
3. l'état des trompes, plus spécialement la perméabilité tubaire, le siège de certaines tumeurs latéro-utérines, parfois même la nature de telle tumeur annexielle, l'uni ou la bilatéralité des lésions salpingiennes et enfin la découverte possible de la cause de la stérilité chez la femme.

En raison de sa simplicité, de la précision des résultats obtenus, de son innocuité absolue, à condition qu'on observe les précautions d'asepsie et qu'on s'absteinne d'intervenir dans les cas d'hémorragies, d'infection génitale en activité, et de suspicion de grossesse, l'exploration radiologique de l'appareil génital mérite de prendre place au rang des procédés d'examen courant.

ABCÈS OSSIFLUANT RÉTRO-PHARYNGÉ.—O. Frenette et J. Hallé.

Le mal de Pott cervical reste une rareté clinique devant laquelle on hésite à poser un diagnostic, à ses débuts. Il faudra penser au torticolis, à l'arthrite cervicale aiguë, à l'arthrite sèche déformante, au cancer et à la syphilis. Lorsque l'abcès ossifluant rétro-pharyngé aura apparu, le diagnostic pourra être établi plus sûrement, mais encore faudra-t-il souvent le concours de la radiographie pour déceler un mal de Pott cervical concomittant et dès lors nier l'abcès rétro-pharyngien banal et le cancer du pharynx.

L'observation du malade qui fait l'objet de cette présentation, révèle que A.M. est admis à l'Hôpital du St-Sacrement le 16 juin 1942, sous un diagnostic de cancer probable du pharynx. Il est vu le lendemain dans le Service de l'Oto-rhino-laryngologie. Son aspect général est celui d'un homme amaigri, fatigué, dyspnéique. La voix est nasillarde, la déglutition très douloureuse. On ne constate aucun signe clinique externe, mais la paroi pharyngée postérieure apparait rouge, tendue, saillante. La tuméfaction occupe celle-ci, faisant tomber le voile du palais et rétrécissant considérablement la lumière du pharynx. Un diagnostic d'abcès rétro-pharyngien est alors porté, en même temps qu'une radiographie est demandée. En outre des limites de l'abcès, celle-ci fait voir un pincement entre la troisième et quatrième vertèbres cervicales. A la suite d'une ponction, une injection de lipïodol est faite dans le sac et une seconde radiographie permet de bien voir une fistule atteignant le quatrième espace de la colonne cervicale et délimitant un tubercule en voie de caséification dans le tissu spongieux du corps de la troisième vertèbre cervicale. Il s'agissait bien là d'un abcès ossifluant chez un pottique, souffrant d'un mal de Pott cervical depuis plusieurs années.

A PROPOS D'INFARCTUS DU MYOCARDE (CONSIDÉRATIONS SUR LE PRONOSTIC.)—R. Lemieux et G. Drouin.

D'après G. K. Mallory, P. D. White et J. Salcedo-Salgar (*American Heart Journal*, vol. 18, déc. 1939, no. 6) qui ont publié une communication originale basée sur l'étude anatomo-clinique de 72 cas d'infarctus du myocarde dont l'âge s'échelonnait régulièrement de 1 à 28 jours, de 1 à 8 semaines, de 1 à 12 mois, et de 1 à 4 ans, l'aspect histologique permet de fixer l'âge de l'infarctus, les petits infarctus sont complètement cicatrisés au bout de un mois, et les grands infarctus suffisamment, sinon complètement, cicatrisés au bout de deux mois.

La distinction entre petits et grands infarctus n'étant pas toujours possible cliniquement, il n'est pas sans intérêt de savoir que certains examens de laboratoire peuvent renseigner sur l'évolution et le pronostic, suivant un travail publié par F. H. Shillito, F. L. Chamberlain et Robert L. Lévy (*Journal of the American Medical Association*, vol. 118, no. 10, march 7, 1942).

En milieu hospitalier, il est suggéré de:

1. Noter la vitesse du pouls, le degré de la température rectale, et les chiffres de la tension artérielle tous les jours.
2. Enregistrer un électrocardiogramme et demander la leucocytose tous les deux jours pendant la première semaine, puis une à deux fois par semaine.
3. Mesurer la vitesse de sédimentation globulaire tous les jours au cours de la première semaine, ensuite une à deux fois par semaine.
4. Mesurer la pression veineuse deux fois par semaine.

A domicile, il suffirait à la rigueur, le deuxième ou troisième jour, pour confirmer le diagnostic et prévoir le pronostic immédiat, de connaître le résultat de la pression veineuse, du tracé électrocardiographique, de la leucocytose et de la vitesse de sédimentation globulaire; ultérieurement, on pourra se contenter de mesurer une à deux fois par quinze jours la vitesse de sédimentation globulaire dont la courbe indiquera à quel moment on sera autorisé à fixer la fin du séjour au lit.

Correspondence

Serological Tests for Syphilis

To the Editor:

The Editorial on "Serological Tests for Syphilis" in the May number of the *Journal*, signed by Dr. Arnold Branch, is most timely and draws attention to a matter of great importance. In order to keep the record straight I feel impelled to point out two omissions. The first of these is to be found in the reference to the recommendations of the Conference of Provincial Laboratory Directors convened in Ottawa last June. According to the Editorial they recommended that "sera that react positively with the preliminary precipitin test are then repeated with a recognized complement fixation test. . . ." whereas, according to the Minutes of the meeting, the advice was that such sera be retested, using not only a comple-

ment fixation test but also a diagnostic flocculation test. They went further and advised that when these tests both give weakly positive reactions the specimen should be reported "Doubtful—Please Repeat"; and when one is positive and the other negative or doubtful the report should read—"Please Repeat". This insistence that the specimen must be definitely positive with two different types of test was considered to be an important safeguard against the hazard of false positives.

The second and more serious omission is the absence of any reference to the work done and projected for the further standardization of serodiagnostic tests in Canada. This matter has received the attention of the Dominion Council of Health and of the Canadian Public Health Association. During the winter of 1940-41, the first action was taken when a survey of the serodiagnostic work being done by the nine provincial laboratories and by the Public Health Laboratory at St. John's, Newfoundland, was conducted by the Laboratory of Hygiene of the Department of Pensions and National Health. In the following year a similar survey of the work of the Department's hospital laboratories was carried out.

These surveys met with a very favourable reception by the Directors, and it was found, as might be expected, that a high standard of practice was being maintained. However, it was also found that most of the laboratories had their difficulties. It was decided, after further consultation with the Laboratory Directors, that it would be useful to make arrangements in the Laboratory of Hygiene of the Department to:

(*a*) Repeat the surveys of performance of syphilis serodiagnostic tests at suitable intervals;

(*b*) Coach laboratory personnel with a view to establishing uniform methods;

(*c*) Offer a consultative service to diagnostic laboratories;

(*d*) Manufacture, standardize and distribute reagents to be used in the performance of strictly specified tests; and

(*e*) Conduct research and keep in touch with developments in the field.

The scheme received official endorsation with the approval of an Order-in-Council (P.C. 73/6073), July 14, 1942. This Order-in-Council authorized the expenditure of $12,000 during the fiscal year 1942-43 for the distribution of antigens and the training of personnel to carry out the projects outlined above. It is contemplated that adequate provision will be made to carry on the work during the fiscal year 1943-44.

In October 1942 the Department of Pensions and National Health, through the Laboratory of Hygiene, made available to all provincial laboratories, free of charge, antigens for the performance of the Kolmer complement fixation and Kahn precipitation tests. At present these antigens are being purchased from the authors of the tests. This is a temporary expedient which will be replaced by our own manufacture as soon as arrangements are completed.

In the meantime, the Department has been fortunate in securing the services of R. H. Allen, Ph.D., M.D., who has joined the staff of the Laboratory of Hygiene for the purpose of heading up this work. Although a number of technical details remain to be ironed out it can be said that Dr. Allen has made considerable progress in getting the scheme under way.

When this plan is in full operation it is our intention to concentrate on the standardization of two or three basic diagnostic tests. These will be chosen in consultation with the Directors of the participating laboratories. It is to be understood, of course, that this standardization of basic tests does not preclude the parallel exploration of any other tests which arouse the interest of the participants. Revision of the basic tests will be made only after further consultation with the Directors.

I think you will agree, Mr. Editor, that a discussion of syphilis serology, as practised in Canada, is incomplete without mention of this pioneer effort.

G. D. W. CAMERON, M.D.,
Chief, Laboratory of Hygiene.
Ottawa, April 11, 1943.

Special Correspondence

The London Letter

(From our own correspondent)

NATIONAL HEALTH SERVICE

Although no details of the Government's proposals have been made public, consultations between the Ministry of Health and the medical profession have begun and certain deductions can be made from the statements of Government spokesmen.

First, it is clear that a national health service, compulsory and freely available to all, is what is contemplated but that every effort will be made to retain the twin principles of "free choice of doctor" and "free choice of patient". Private practice will not necessarily disappear, but as already pointed out by Sir William Beveridge himself, with everyone paying for a medical service it seems inevitable that those who wish to make private arrangements at additional cost will be a diminishing few.

Secondly, it has been made clear that the basic organization of the service is to be through enlarged local authorities (*i.e.*, elected bodies) with medical advisory members. Whether this

is still open to negotiation is not clear and already the British Medical Association has indicated that it intends to oppose this aspect of the scheme in a whole-hearted fashion.

Voluntary hospitals are to be left to continue with Government grants and presumably some degree of Government control, and there is to be some closer collaboration and standardization of the voluntary and municipal hospital methods. Consultants and specialists will presumably be much more closely attached to their hospitals, receiving payment for services rendered, but this like many other details is still speculative.

A representative group of the profession is meeting the Minister of Health in what is termed the discussion phase with promises of careful consultation with the whole profession, including those in the Services, before negotiations open. Meanwhile the subject of professional freedom is much under discussion. The antithesis between "autocratic" medicine, which means service under a local authority, and "democratic" medicine, which means working in the voluntary hospital system, is being stressed. The terms used are strange when it is remembered that a local authority is democratically elected whereas a voluntary hospital board of management seldom is. But the freedom of the medical man is alleged to be quite different in the two systems, and granted this point it is easy to see why extension of local authority control is feared more than anything else.

INDUSTRIAL HEALTH

The Minister of Labour has appointed an advisory committee with nine medical members to help him on all questions of industrial health. In the words of the Minister the object is to make work healthier, safer and pleasanter. The Industrial Health Research Board, dating from the last war, is to continue its function of long-term inquiries, but the new committee is to tackle everyday problems, to make the best use of every new discovery, especially regarding such matters as lighting and ventilation, and it is to concern itself also with such subjects as nutrition. The great industrial expansion has brought many medical practitioners into industry for the first time as part-time works doctors and there is better liaison than ever before between these doctors and the general medical practitioner.

It seems a good moment to cement this relationship and a big three-day conference on industrial health is being held just as this letter is being completed. It is hoped that hours of work will be considered for there is still great ignorance on the part of employers and even Government officials of the evil effect upon health and on output from too long hours and too few holidays. The present-day civilian doctor could add his testimony from his own personal experience on this score and it is lamentable when the greatest output of the greatest work is required to finish the war that fatigue is allowed to impair efficiency. The delusion that extra work can be obtained by increasing the hours of labour dies hard.

HEALTH EDUCATION

When the Ministry of Health was formed in 1919 one of its duties was clearly laid down to be the dissemination of knowledge about health. Until recent times there has been little sign of this being carried out, but since the war posters and pamphlets on such matters as diphtheria prophylaxis, the dangers of droplet infection, food in wartime and venereal disease have been issued officially. The "radio doctor" has also set a new standard for a type of health talk which undoubtedly reaches a wide audience, eager for advice.

The Central Council for Health Education has undertaken new duties, especially as regards the campaign against venereal disease, and has issued the first number of its new quarterly publication called *Health Education Journal*. A recent conference on venereal disease organized by this body brought the Minister of Health and the Archbishop of Canterbury on to the same platform, to give, it is true, different points of view but fundamentally to raise the same issue, namely that health is to be attained by the dispelling of ignorance—one of Sir William Beveridge's "five giants".

ALAN MONCRIEFF

London, April, 1943.

Canadian Medical War Services

Immunization Measures in the R.C.A.F.

Group Captain J. W. Tice, Director of Medical Services (Air) said recently that immunization measures have banished from the R.C.A.F. both tetanus (lockjaw) and typhoid fever, which ranked with venereal disease as the great scourges of armed personnel during the first World War. There has not been a single case of tetanus in the R.C.A.F. since the outbreak of war, and only four cases of typhoid fever — all new recruits — which represented 0.02% of the total of communicable diseases in the R.C.A.F. to date.

There was an outbreak of diphtheria in the spring of 1941 that quarantined the training school at St. Thomas where there were sixty-two cases in eight weeks, with one death. The outbreak disrupted posting arrangements, as airmen could not be moved from the Station for advanced training at other centres, and more junior airmen could not be brought in for training. Tests which had been conducted during the preceding months showed that

roughly 50% of all healthy young men were susceptible to diphtheria with its deleterious effect on heart muscles, nerves and kidneys. As the result of its studies, the Air Force on June 26, 1941, put into effect the widespread diphtheria toxoiding plan which has been found so successful. In the twenty months since the R.C.A.F. toxoiding plan started, only 32 cases of diphtheria have developed among all the British Commonwealth Air Forces training in Canada, bringing the total of 123 cases of diphtheria in the Air Force since the beginning of war, only 0.68% of the total of all communicable diseases in the Air Force.

Group Captain Tice stressed the greatly superior effectiveness of immunization to quarantine. "Attempts to control communicable disease by quarantine have been found, as in civil experience, to be quite inadequate," he said. "The frequent movement of Air Force Personnel from unit to unit and province to province multiplies the difficulties in applying quarantine measures which disrupt the training program, frequently to little avail. In war time health measures must be practical. Measures whose results are uncertain or which interfere significantly with the training or operational activities of troops must be avoided."

The x-ray examination of all applicants' chests preliminary to enlistment in Canada's armed forces has enabled another striking contrast in health records between this and the First World War, which has cost Canada tens of millions of dollars for tubercular patients alone in the past twenty-five years. "The x-ray has been of benefit in discovering tuberculosis which was unknown to the applicant for enlistment and we have been able to advise him and the Provincial Department of Health," said Group Captain Tice. "The examination also has ensured that men in barracks were not infected by tuberculous cases. The value has been demonstrated further by the fact that the incidence of tuberculous cases among R.A.F. personnel not given a chest x-ray, has been found to be 13 times that among R.C.A.F. personnel."

Comparisons of the health of civilians and service personnel emphasize the value of immunization programs. The incidence of scarlet fever in Ontario in 1942 was double that in 1941, but the incidence among Air Force personnel was only half that of the previous year. More than 60% of Air Force cases occurred at points of initial entry before the airmen were inoculated. In one Canadian Province through which a large number of trained airmen pass on their way to theatre of war, the incidence of diphtheria has been extraordinarily high, 160 cases per 100,000 population, compared with a rate of only 18 in the R.C.A.F. There has not been one death from diphtheria since the program was undertaken.

Group Captain Tice said that records at R.C.A.F. Units showed that the average gain in weight for new recruits was 5.4 pounds in three months, and that the average gain for underweight recruits was 7.3 pounds each.

Abstracts from Current Literature

Medicine

Thrombocytopenic Purpura Caused by Sulfonamide Drugs. Gorham, L. W., Propp, S., Schwind, J. L. and Climenko, D. R.: *Am. J. Am. Sc.*, 1943, **205:** 246.

The authors report three cases of thrombocytopenic purpura following sulfonamide drug therapy. One case followed the administration of neoprontosil and sulfanilamide to the same patient. Recovery occurred. The other two patients who developed this complication died. The drug used in one instance was sulfapyridine, in the other sulfadiazine. The total number of instances of thrombocytopenic purpura following sulfonamide therapy reported in the literature is now eight. Half of these eight patients died of the complication. The authors point out the similarity in the chemical structure of these drugs to benzol and aniline, which have long been recognized as hæmatotoxic, and urge that sulfonamide therapy be stopped as soon as there is evidence of bone marrow disturbance. They suggest that frequent platelet counts as well as leucocyte counts should be made while these drugs are being administered. E. S. MILLS

The Comparative Value of High and Low Doses of Sulfadiazine in the Treatment of Pneumococcic Pneumonia. Dowling, H. F., Hartman, C. R., Feldman, H. A. and Jenkins, F. A.: *Am. J. M. Sc.*, 1943, **205:** 196.

The authors have compared the results of treating 79 patients with unusually large doses of sulfadiazine with 81 controls who were given the usual dosage. The high dosage group received 6 grm. initially, followed by 1 grm. every 4 hours, while the controls received 2 cm. followed by 0.5 grm. every 4 hours till recovery or death. There was no remarkable difference either in the mortality or in the incidence of serious complications in the two groups. However, in the high dosage group the temperature fell more rapidly; the hospital stay was 3.4 days less; and the incidence of relapse, spread of the pneumonia, and slow resolution were less than half that in the controls. Toxic reactions were infrequent in both groups and not higher with the higher dosage. The authors are not of the opinion that the higher dosage is justified, in view of the present limited supply of the drug. E. S. MILLS

Myeloid Hyperplasia and Metaplasia Induced by Extracts of Urine from Patients with Myelogenous Leukæmia. Heinle, R. W., Wearn, J. T., Weir, D. R. and Rose, F. A.: *Ann. Int. Med.*, 1942, **17:** 902.

The authors demonstrate that extracts of urine from patients with chronic myeloid leukæmia produced myeloid hyperplasia and metaplasia in guinea pigs with much greater frequency than did extracts from patients not having chronic myeloid leukæmia. Three different extraction methods and four different extracts are described. Whether the substance is a normal metabolic product present in excess in the urine of chronic myeloid leukæmia patients or whether it is an abnormal product normally present in urine, is not known. If it is an excess of normal substance, such excess may be due to overproduction of the substance or to decreased production of some normal neutralizing substance.

S. R. TOWNSEND

Surgery

Left Subphrenic Abscess. "Abcès sous-phrénique gauche". Neuhof, H. and Schlossman, N. C.: *Surg., Gyn. & Obst.*, 1942, **75:** 751.

La différence anatomique fondamentale entre l'abcès sous-phrénique gauche et le droit est que l'expansion de ce dernier se trouve limitée par un organe solide, relativement immobile: le foie et ses tributaires—veine cave et conduits hépatiques—alors que du côté gauche nous trouvons des organes plus mobiles: rate, estomac, colon, prêts à favoriser une plus large extension de la suppuration qu'à droite. Cela suffirait à expliquer fréquence et indice de mortalité plus élevés à gauche qu'à droite.

Les manifestations cliniques de l'abcès sous-phrénique gauche, généralement vagues et dispersées, apparaissent assez tardivement dans le cours du mal. La présence indirecte de manifestations thoracico-abdominales a souvent plus de signification que les signes directs de l'abcès sous-phrénique lui-même. Il est important de procéder à des radiographies du diaphragme, surtout en position latérale et oblique, afin de déceler la présence d'une ombre d'origine inflammatoire et de déterminer l'exacte situation du diaphragme et sa mobilité.

Une aspiration exploratrice, basée sur la radiographie, est essentielle afin de préciser le diagnostic et de décider de la manœuvre opératoire. Les auteurs recommandent une intervention chirurgicale sous-diaphragmatique, quand il s'agit d'un abcès sous-phrénique gauche de type "abdominal". Une intervention trans-pleuro-diaphragmatique est conseillée pour l'abcès, type "thoracique". Il est préférable de faire cette dernière opération en un seul temps. A cause de leurs différences étiologiques et pathogéniques, on ne saurait confondre en importance l'abcès sous-phrénique droit et gauche. Ce dernier, causé par des lésions le plus souvent irrémédiables, maintient un indice élevé de mortalité. PIERRE SMITH

The Effect of Various Blood Substitutes in Resuscitation after an otherwise Fatal Hæmorrhage. Ivy, A. C., Greengard, H., Stein, I. F., Godins, F. S. and Dutton, D. F.: *Surg., Gyn. & Obst.*, 1943, **76:** 85.

A series of experiments on dogs has led to some interesting conclusions on blood substitutes. The dogs were bled in a single massive hæmorrhage, to produce a uniform degree of shock. Blood loss varied from 45 to 78% of the total volume and produced a condition which led to death in most of the controls. Very detailed accounts of results are given. The main conclusions are:

1. Intravenous saline reduced mortality after single massive hæmorrhage from 84 to 58%.
2. Pooled serum reduced mortality to 26%.
3. Sodium citrate is toxic. This has long been known. Caution must be exercised in giving citrated plasma or whole blood in large quantities (more than 1,200 c.c.) to patients who have lost from 40 to 50% of their blood, especially if the transfusion is given rapidly. In this series 35 of 50 dogs so transfused died rapidly. Plasma used contained citrate in concentration of 0.25%.
4. Heparinized plasma reduced mortality from 84 to 6%. It was the most effective blood substitute tested. Such results indicate that replacement of erythrocytes is not necessary for survival in massive hæmorrhage.
5. Most gelatins and all gum acacia and pectin solutions tested caused pseudo agglutination which, after a massive hæmorrhage and a large transfusion, had a lethal effect. J. R. LACROIX

Fate of Procaine in the Human Body after Subarachnoid Injection. Goldberg, A. *et al.*: *Arch. Surg.*, 1943, **46:** 49.

The authors embark on a program designed to develop and utilize trustworthy techniques which would enable them to trace the course of the drug, determine what changes, if any, it underwent and find the site and the mechanism of these changes.

They believe that sufficient information has been gained to assist materially in the understanding of spinal and local anæsthesia induced by procaine hydrochloride. They developed a delicate analytic method for the determination of procaine in the various body fluids. As procaine is rapidly detoxified, several supplementary procedures were developed so as to distinguish each of the products of detoxication separately. The technique of the method is outlined. Their experiments have been limited to the blood of human beings and dogs. The great difference between the activity of canine and human blood makes the value of experiments on dogs dubious. The authors conclude that by means of new chemical techniques it is shown that procaine within the subarachnoid space remains essentially unchanged. The fall in concentration of procaine which is responsible for the wearing off of anæsthesia is due to vascular absorption. Once in the blood stream, procaine is rapidly detoxified by an enzyme. An average of 90% of all the injected procaine is excreted in the urine in the forms of products of detoxification.

G. E. LEARMONTH

Æsthetic Considerations in Surgical Operations from Antiquity to Recent Times. Kunstler, W. E.: *Bull. Hist. Med.*, 1942, **12:** 1.

Æsthetic considerations in surgical operations can be found at any time since surgery developed. The writer has looked over almost two hundred manuscripts, incunabula, and old textbooks covering the period of 3,000 B.C. up to the middle of the last century, finding many suggestions of techniques which are still in use in our times and which are often considered as new inventions. He shows particularly that directions for incisions played a great rôle in making scars less noticeable. The right choice of site of incisions in the removal of tumours can prevent disfigurement. An accurate suture technique prevents scars from looking awkward or from breaking up again. Exact setting of fractures like that of the collarbone restores the normal anatomical contours. Gentle working on living tissue with special instruments does not interfere with wound healing. Application of anatomical and physiological principles are important in addition to the right choice of surgical methods, as many diseases like cold abscesses, lachrymal fistula, varicose veins, etc., can be successfully treated without mutilating the human body. There are many other important points mentioned which seem today to be elementary. All these efforts of surgeons in the past deserve more appreciation, as they could not take advantage of our modern aids such as x-rays, anæsthesia, detailed laboratory technique, etc.

The author comes to the conclusion that study of the history of medicine not only gives an interesting view of the standard of surgery at a particular time, but also prevents the description of so-called new methods of writers, only to find later, that their idea was already well-known a few hundred or a few thousand years before their time.

Gynæcology and Obstetrics

The Importance of the Rh Blood Factor in Erythroblastosis. Potter, E. L., Davidsohn, I. and Crunden, A. B.: *Am. J. Obst. & Gyn.*, 1943, **45:** 254.

The introduction of the Rh antigen into an individual in whom it is not normally present may result in the production of anti-Rh agglutinins. The introduction of the antigen may be accomplished by transfusion with Rh+blood or by passage through the placental barrier of Rh+cells from the fetal circulation. If anti-Rh agglutinins are produced the subsequent introduction of large amounts of blood containing the Rh antigen may result in a fatal reaction. If anti-Rh agglutinins are produced, a subsequent pregnancy may terminate unfavourably because agglutinins transferred to the fetus may cause erythroblastosis.

In suspected cases of erythroblastosis the absence of

the Rh-antigen in the maternal blood, associated with its presence in the paternal blood, lends support to the diagnosis. ROSS MITCHELL

Intracyclic Bleeding. Greenblatt, R. B.: *Am. J. Obst. & Gyn.*, 1943, **45:** 299.

The ovulation syndrome of intracyclic bleeding may be so annoying as to require attention. The administration of testosterone propionate parenterally in 10 to 25 mgm. doses at weekly intervals alleviated the syndrome. Methyl testosterone administered orally in 5 to 10 mgm. doses throughout the intermenstruum proved just as effective in minimizing and arresting midinterval bleeding or pain without interfering with ovulation.
ROSS MITCHELL

Comments on the Third Stage of Labour. Brown, R. C., O'Sullivan, J. V. and Sanctuary, J.: *J. Obst. & Gyn. Brit. Emp.*, 1942, **49:** 646.

Separation of the placenta always takes place in the centre. The terms Schultz and Mathews Duncan should be confined to describing the methods of expulsion.

The method of expulsion is determined by the situation of the placenta. If the placenta is situated low in the uterine wall premature separation of the lower edge may take place. In cases of placenta prævia the placenta is usually expelled by Mathews Duncan's method and this is why these cases frequently suffer from post-partum hæmorrhage. Earlier manual removal of the placenta is advised in cases of post-partum hæmorrhage.
P. J. KEARNS

Degenerative Vulvovaginitis Associated with Œstrogen Imbalance. Shute, E.: *J. Obst. & Gyn. Brit. Emp.*, 1942, **49:** 482.

Several points in the management of these cases should be stressed. The patients having low blood œstrogen values usually respond quite well to œstrogens given by any route, but, perhaps, do best on suppositories. As has been said, the effect is prompt, developing within a week or two, and lasts for weeks or months or even longer. There is a tendency for the condition to recur, when it responds quite as well as at first to the same therapeutic measures. If œstrogens are used for the high œstrin cases the vulvovaginitis may be aggravated and become very distressing. However, this is not always so, indicating either that our qualitative œstrin assay is sometimes fallacious or that such patients are occasionally healed by thickening the epithelium with or without cornification.

In the high œstrin cases the patients need such an antiœstrogen as thyroid extract or vitamin E. The author has not tried such others as progesterone, chorionic gonadotrophin or testosterone propionate. Certain women have an idiosyncrasy to wheat germ oil. These must be given synthetic vitamin E or the alternatives mentioned. P. J. KEARNS

Pregnancy Following the Intra-uterine Application of Radium. Mayeur, M. H.: *J. Obst. & Gyn. Brit. Emp.*, 1942, **49:** 542.

A series of 89 patients under 40 years of age who had been treated with an intra-uterine application of radium for non-malignant conditions has been studied to determine frequency of conception after treatment, and the course of their pregnancies. Nine of the patients subsequently became pregnant and had between them 14 pregnancies. Abortion occurred in 57% of these, and in only 5 cases did the fetus attain viability. One patient is still pregnant. In the whole series, and out of 14 pregnancies, only 2 live children were born. The cause of this wastage was first the high incidence of abortion, and secondly dystocia during labour.

Severe dystocia may result from delay in the dilatation of the cervix in cases in which an intra-uterine application has been made. Six such cases were described. The cause of the dystocia was cervical fibrosis. Whether it can be avoided by using only a short intra-uterine tube and confining the irradiation to the top half of the uterus is a point worthy of consideration.
P. J. KEARNS

Anæsthesia

A Critical Analysis of the Use of Intravenous Morphine. Presman, D. and Schotz, S.: *Anæsthesiology*, 1943, **4:** 53.

The authors point out that the use of morphine intravenously has been employed by only a minority of practising physicians and surgeons and that the majority seem to be unaware of the great scope afforded for both diagnostic and therapeutic purposes by the method. They have kept careful records in one hundred unselected cases where intravenous morphine was administered. Their technique employs either morphine gr. 1/6 or 1/4 dissolved in 2 c.c. sterile water and injected slowly through a fine hypodermic needle at the rate of ½ c.c. per thirty seconds. It must be remembered however that these adult dosages must be individualized and they have varied from ⅛ grain to as much as ½ grain in the same amount of water. During the injection the patient is questioned concerning side effects such as dizziness, tinnitus, nausea, etc. In their conclusions the authors state that intravenous morphine is definitely indicated for the following conditions. (1) As a preoperative medication for general and spinal anæsthesia when the customary subcutaneous injection of morphine was not given because of an emergency or oversight. (2) As a preoperative medication for spinal anæsthesia if the patient is still apprehensive and upset on entering the operating room in spite of previous preoperative sedation. (3) As a sedative for restlessness and discomfort during a spinal anæsthesia and for pain while the surgeon is closing the fascial and skin layers of the incision. (4) As a routine preanæsthetic for all operations performed under local infiltration or nerve blocks. This especially applies to thyroidectomies done under local anæsthesia. (5) For gastroscopy, bronchoscopy, and in selected cases for cystoscopy and retrograde pyelography. (6) For debridement of lacerations and burns when a general anæsthetic is unnecessary or undesirable. (7) For changing of painful dressings. (8) For severe biliary and renal colic. (9) For marked dyspnœa due to coronary failure or pneumonia. (10) For severe pain due to coronary artery disease. (11) For the differential diagnosis of the acute surgical abdomen.

They also add that intravenous morphine can well be used in the present-day world conflict as a rapidly acting analgesic in first aid and evacuation surgery and for emergency surgery. F. ARTHUR H. WILKINSON

Oto-Rhino-Laryngology

Desquamative Otitis Externa in Malta. Dagett, W. I.: *J. Laryn. & Otol.*, 1942, **57:** 427.

The author describes the diagnostic and treatment procedures followed by him in 193 cases of desquamative otitis externa. The condition is seasonal in hot humid climates. There is swelling and reddening of the meatal skin of the ear, the drum may be slightly injected, and there is a mass of cheesy debris filling the deep meatus and obscuring the drum. There may also be a thin straw coloured discharge. The differential diagnosis depends on finding the drum practically normal, normal hearing tests and absence of a history of otitis media. The bacteria found are mainly, diphtheroids, *B. pyocyaneus*, and *B. proteus*. No accessory etiological factors were found. Treatment was to clear away the desquamated skin very carefully then to insert a wick of gauze soaked in the following mixture: lead acetate gr. 10; aluminum acetate dr. 1; aq. menth. pip. oz. 1. This formed a protective coagulum over the skin surface and was repeated for 2 to 3 days. Then an insufflation of boracic powder 99%, iodine 1% was blown over the meatal surface. Sulfonamides were found useless. 63% of the cases were cured in four days, 29% more were cured within ten days while 8% took longer.
GUY H. FISK

The Teleradium Treatment of Intrinsic Cancer of the Larynx. Lederman, M. and Mill, W. A.: *J. Laryn. & Otol.*, 1942, **57:** 471.

This paper is a discussion of 35 cases of carcinoma of the larynx treated by radium. Nine of these were recurrences following previous treatment by surgery or x-ray, while 26 had been untreated. A detailed statistical table of all the cases is provided. These carcinomata arose from (1) the true vocal cords, (2) the false vocal cords and ventricles, (3) the subepiglottic region and (4) the anterior and posterior commissures. Disease involving the suprahyoid epiglottis or the pharyngeal surface of the arytenoid is excluded. Treatment used by the authors is the irradiation by radium beams of two small fields over the thyroid alæ. Each field receives 300 to 350 r per treatment. The treatments are given daily six days a week for from 4 to 6 weeks. The authors aim at giving a total of 7,000 r in the course of treatment. Tracheotomy is avoided unless absolutely essential to save life. Of the 15 cases treated up to 1937 and observed for 5 years 7 are alive and well and one is untraced. GUY H. FISK

Orthopædics

The Pathological Changes in Recurrent Dislocation of the Shoulder. Best, F. C. and Inman, V. T.: *J. Bone, Joint Surg.*, 1943, p. 595.

These authors have set out to study the essential pathology of recurrent dislocation of the shoulder and to see whether the process described by Bankhart is true. Their investigations of ten cases found in each case a tear of the glenoid labrum, but in addition a defect in the postero-lateral area of the head of the humerus and a stubbing of the bony glenoid rim. The postero-lateral defect of the head of the humerus only shows on x-rays if the humerus is in full internal rotation.

As regards treatment they follow the operative repair of the defect as carried out by Bankhart with good result. Eight of ten patients were followed for 18 to 36 months and 7 had excellent results. The eighth, an epileptic, was a failure due to recurrent severe trauma.
H. F. MOSELEY

Therapeutics

The Effects of Ascorbic Acid in Relation to Lead Absorption. Evans, E. E., Norwood, W. D., Kehoe, R. A. and Machle, W.: *J. Am. M. Ass.*, 1943, **121:** 501.

Beneficial effects have been claimed following the administration of vitamin C to lead workers. The benefits are said to be a reduction in symptoms of exposed workers and a decrease in the lead content of the blood and urine. The present study deals with workers in a plant for the manufacture of tetraethyl lead. These workers have been under close supervision for a number of years and records of blood and urinary lead, of stippled red blood cells and of blood pressure over many months have been kept. Seventy-two workmen form the basis of this study. Half of them were given 100 mgm. of ascorbic acid daily for a year, the other half received no medication. Previous records of these men indicated that the two groups were comparable as regards excretion of lead, number of symptoms reported and levels of lead in the blood. The average age for the ascorbic acid group was 37.3 years and for the control group 36.0 years. The average time of employment was 9.3 and 8.1 years respectively.

Before giving ascorbic acid studies were made to determine the state of vitamin C nutrition, and it was found that by present standards it was relatively poor. The experimental results with respect to the lead concentration of the blood and urine of the ascorbic acid group and the control group are given in the accompanying Table:

	1939 *year prior to treatment*	1940 *year of treatment*	Control Group 1939	Control Group 1940
Average lead in mgm. per 100 c.c. of whole blood	0.051	0.043	0.043	0.046
Average lead in mgm. per litre of urine ..	0.105	0.103	0.096	0.107

The differences are so small as to be considered insignificant.

The authors conclude, "No reason has been found for recommending the use of ascorbic acid to minimize the effects of lead absorption." FRANK G. PEDLEY

Pathology and Experimental Medicine

Histologic Analogy of Bronchial Adenoma to Late Prenatal and Early Postnatal Structures. Harris, W. H., Jr.: *Arch. Path.*, 1943, **35:** 85.

Bronchial adenomas are said to comprise 6 to 10% of all bronchial tumours. Markedly vascular tumours occur in which the type cell closely resembles the lymphocyte. These tumours, Harris believes, arise from the mesoderm and cannot be correctly classified as adenoma without suitable qualification of the term. In other tumours the growth is mainly composed of large polyhedral cells showing glandular arrangement and having an endodermal origin. However, benign tumours do occur in which both these types of tissue are seen and these may be called "mixed tumours". Various theories of origin of these tumours have been suggested—that they arise from the bronchial mucous glands, from the duct epithelium of these glands, from maldeveloped embryonic bronchial buds, or from glandular "rests". Since it has been suggested that these tumours may originate from embryonic and fetal remnants, Harris examined transverse sections of the trachea just above the bifurcation, and of the main bronchi, one centimetre below their origins, in fetuses ranging in age from 7 months to maturity and in infants up to 3 months of age. In all, 23 cases were studied. In these sections, the bronchial mucous glands were seen to occur beneath the mucosa and also more deeply between the cartilaginous rings. The lining epithelium of many of the glandular acini did not show the regularity of cells and of cellular arrangement seen in sections from more mature infants and, in the opinion of the author, these acini did not appear unlike the poorly developed glandular formations seen in some benign bronchogenic tumours. In studying the vascularity of the bronchial walls, Harris noted that the vascular channels appeared more like sinuses and while they were most numerous in the submucous layer, they also occurred in lymphoid tissue, contiguous to the bronchial wall. In some sections, this vascularized lymphoid tissue extended deeply into the wall of the bronchi. The author stated "that bronchogenic adenoma may closely simulate both the cellular pattern and vascularity of such lymphoid developments". Harris believes that it is conceivable that tumours may originate from these immature structures of both glandular and lymphoid type and hence may be extramural or intramural in location and may protrude into the lumen. H. L. FOSTER

Latent Primary Carcinoma. Gewanter, A. P., Mitchell, N. and Angrist, A.: *Arch. Path.*, 1943, **35:** 66.

Latent carcinoma is defined by the authors as "a cancer whose metastasis causes the initial symptomatic picture". In a series of 2,514 autopsies, they found 25 instances of latent cancer in a total of 391 cases of carcinoma, an incidence of 5.9%. In this group, the common primary sites were lung (8 cases), pancreas (5 cases), and stomach (3 cases). Other, less common primary sites included prostate, uterus, kidney, ovary, male breast and testis. The most frequent locations of metastases giving rise to symptoms were pleura and peritoneum, central nervous system, long bones, lymph

nodes and liver, and, less commonly, lung, intestines, ovary and adrenal. The authors concluded that lung, pancreas and stomach are common sites of origin of carcinoma and of latent carcinoma. However, the latency is not determined by the frequency of the occurrence of tumours, since tumours arising in rectum, sigmoid and bladder are common, yet these are not frequent sites for latent carcinoma. Factors which contribute to latency are the inaccessibility of tumours of internal viscera with accessible secondary growths, the early invasion by tumour of blood and lymphatic channels, and the size and strategic locations of secondary growths. H. L. FOSTER

Radiology

Excretory Urography as a Test of Urinary Tract Function—Carman Lecture, 1942. Pendergrass, E. P.: *Radiology*, 1943, **40:** 111.

This is a detailed and exhaustive article reviewing (1) some of the phases of anatomy and physiology that should be considered in doing a urographic study; (2) the methods used to record the clearance and transportation of the contrast medium; (3) suggestions concerning the interpretation thereof. Further progress certainly will occur and urokymography provides one method for future investigation.

Excretory urography is recognized as a definite contribution to urological radiography. At present, it is an unsurpassed roentgen method of estimating total urinary tract function if our interpretation is based on physiological principles. R. C. BURR

The Betatron. Kerst, D. W.: *Radiology*, 1943, **40:** 11.

This paper is concerned with a new method for electron acceleration and the author suggests that the type of accelerator used, the betatron, should find worthwhile applications in deep therapy. In this instrument the energy is transferred to electrons by the accelerating effect of a time-varying magnetic field. Since a betatron is a powerful magnet, between the poles of which the electrons circulate in essentially one plane the apparatus looks somewhat like a small cyclotron. It operates, however, with alternating current instead of direct current, and the process of acceleration is entirely different from that in the cyclotron. The betatron can accelerate particles whose velocity is very close to the velocity of light, such as electrons with energy in excess of half a million volts. Particles accelerated in a cyclotron, on the other hand, must have a velocity much less that of light, and therefore only heavy positive ions can be accelerated in it to appreciable energies.

The name betatron, which is now in general usage among physicists, was chosen for the magnetic induction accelerator, since it seems likely that the most useful applications of the betatron will involve the production of high-speed electrons or beta rays, as they are known in nuclear physics. R. C. BURR

Hygiene and Public Health

Use of Ultraviolet Radiation in Reduction of Respiratory Cross Infections in a Children's Hospital. Chant, E. R., Doyle, M. E. and Tisdall, F. F.: *J. Am. M. Ass.*, 1943, **121:** 908.

Infants treated in open six-bed rooms or in a room with 8-foot partitions developed 2 to 3 times as many respiratory infections as babies in a room divided into cubicles with partitions running to the ceiling, a curtain of ultraviolet radiation across their entrances and an air-changing system. When the ultraviolet lamps were turned off and the progress of the babies in the room with complete partitions and an air-changing system was compared with that of other babies in the room with partial partitions, it was found that those in the latter type of room had only slightly more infections. The curtains of ultraviolet radiation between the babies were therefore the major factors in the decided reduction of respiratory cross infections described in conclusion 1. Two hundred and seventy-six strains of group A hæmolytic streptococci and pneumococci were recovered from the staff and the babies. In only 18 instances was the transfer of these organisms from patient to patient, from staff to patient, or *vice versa*, demonstrated. Infants treated in rooms in which the upper air was irradiated showed approximately the same number of infections as babies treated in rooms similar but without ultraviolet radiation. The doors and windows in these rooms were frequently left open. Premature infants treated in the regular premature room had nearly twice as many respiratory infections as similar infants in a room in which the upper air was irradiated. The doors and windows were kept closed in these rooms. During the last 2½ years the progress of 682 babies has been followed; 258, or 38% have developed respiratory infections, many of which were mild. FRANK G. PEDLEY

Obituaries

Dr. A. Grant Fleming. Canada has lost an outstanding public health leader and a widely beloved citizen in the death of Dr. A. Grant Fleming. His eminent scientific attainments, zeal for public service, wide humanitarian interests, keen common sense and captivating personality were unselfishly dedicated to human welfare. As a medical statesman, he contributed to signal advances in the United States as well as in the Dominion. He was affectionately known as "Grant" to a multitude of friends and colleagues. His passing creates an acute sense of void in many hearts.

No fitting tribute could be made to Grant Fleming without making reference to the wide sweep of his activities, to the imprint he made upon preventive medicine, and to his qualities as a man.

From the vantage point of McGill University as a former Dean of Medicine, and as Director of the Department of Public Health and Preventive Medicine, he was a constructive force in research and in medical education. Through his attachments to numerous local and national health agencies, and to American Foundations, he enriched public health programs throughout the Continent. As Medical Director of the Bell Telephone Company of Canada, he laid the groundwork for far-reaching advances in industrial medicine. In addition to these many responsibilities, he conducted surveys, furnished consulting services to the Federal Government and to Provincial Governments, wrote scientific articles and was active in the field of public education. At the time of his death, he was attached to the Canadian Army in charge of preventive medicine. With such an amazing record of service, Dr. Fleming occupied a unique position in Canadian medicine.

In his chosen field of public health, Dr. Fleming will be remembered for three outstanding contributions; the linking of mental hygiene with physical hygiene; the combining of public health with social welfare activities; and the effecting of a partnership between preventive and therapeutic medicine.

Dr. Fleming was identified with the mental hygiene movement since its inception more than a quarter of a century ago. He was one of the first men in America to appreciate the fact that, in connection with more than one-third of all human illness, mental and situational factors played a prominent rôle in causation and in determining course and outcome. With this revelation, he became convinced that public health was not attending to its full task if mental hygiene was left out of its program. He attached himself to the National Committee for Mental Hygiene of Canada, made intimate contacts with Provincial Departments of Health, and established a close partnership between mental hygiene and public health. These pioneering efforts led to similar developments in other parts of the world.

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While the laboratory phases of public health appealed to Dr. Fleming as being most significant, he was by nature more attracted to the human and social aspects of this field of endeavour. He became convinced of the enormous significance to health of such factors as housing, living conditions, economic status, recreational and cultural opportunities, degree of health, education and other social influences. And he decided that a health program to be effective should be an integral part of a larger welfare program. With characteristic zeal, he dedicated himself to pioneering along these lines. At McGill University, he stimulated social studies in relation to health. He utilized the findings in promoting constructive programs in Montreal and throughout the country until a Dominion-wide trend was established.

At the beginning of his career, Dr. Fleming viewed with concern the existing tendency of a separation of activities as between preventive and therapeutic medicine. He knew that a comparatively few workers in public health could not possibly be effective in meeting the challenge for the prevention of human illness. It was apparent to him that it was necessary to secure the active participation of the whole body of the medical profession. But there was a serious difficulty that blocked advance in this direction. There was the problem of medical economics—the problem of paying the profession for preventive work. The only solution seemed to be in the direction of organizing a national health program with the funding of physicians from Federal or Provincial sources. And, as a means of working toward this end, Dr. Fleming applied himself to a study of the distribution of medical care and public health services in Canada. This study was published in 1939 and was widely distributed. It was a significant factor in paving the way for constructive legislation that is now receiving attention in Ottawa.

These outstanding achievements of Dr. Fleming were made possible because of the character of the man himself. He was utterly selfless and devoid of any ambition for personal gain or aggrandizement. He was dedicated to one thing only—his work—the improvement of the lot of his fellows. He had a modest and mild disposition, but was fearless and courageous in championing the truth as he saw it regardless of personal consequences. He disliked politics and personal intrigue in medical and other affairs. He was as much interested in the jobs of his colleagues as in his own, and thus, he was a priceless counselor. He was loyal to his friends and to all humanity. He left the world richer because of his ennobling life. His memory will be a constant source of inspiration to his students and co-workers. And thus, his wholesome constructive influence will live on.

APPRECIATION BY C. M. HINCKS

Dr. Charles Cleland Alexander, of Brantford, for a number of years medical officer and medical superintendent of the Brant sanatorium, died at his home in Brantford on May 4. He had been in retirement since 1939.

At the outbreak of the first Great War Dr. Alexander enlisted and served in the Royal Canadian Army Medical Corps throughout. He came to Brantford as a general practitioner in the early part of 1920.

Dr. Alexander was born in Iowa in 1884 and went to Seaforth, Ont., when he was six years old. He attended school there and later taught school in that district for four years before entering the University of Toronto from which he graduated in medicine in 1911. He took postgraduate work in surgery at Cleveland, Ohio. Returning to Ontario, he entered the Gravenhurst Hospital to take postgraduate work in the treatment and prevention of tuberculosis. Leaving there, he practised medicine for a short time in Barrie.

Dr. Herbert Wesley Armstrong, of Fergus, Ont., died on May 5 in his seventy-fifth year. He was a graduate of Trinity University, Toronto (1889).

Dr. Ernest Eugene Bissett, of Windsor, N.S., died on April 14, 1943.

Dr. Bissett was born at River Bourgeoise, Richmond County, son of George H. and Virginia Boudreau Bissett. One of a family of twelve, Ernest Bissett was sent to St. Francis Xavier University for his Arts course and then to Dalhousie, where he obtained his medical degree in 1897. In the Fall of that year he opened a practice in Port Morien, and was for 14 years, with some time out for postgraduate work, surgeon of the Dominion Coal Company for Dominion district. The first years of this practice indicated that a general practitioner in a rural area must have special knowledge and in 1900 he went to New York to take postgraduate work. Returning to Port Morien he was married there, in 1903, to Irene Clinton, daughter of Mr. and Mrs. O. J. Clinton. Dr. Bissett's practice brought him into close association and warm friendship with Dr. E. A. H. McKeen, brother of a former Lieutenant-Governor of Nova Scotia, David McKeen, who was Chief Surgeon of St. Joseph Hospital at the time of its founding. In 1912 Dr. and Mrs. Bissett removed to London, England, where he had two years of postgraduate work at London Hospital.

They returned to Nova Scotia in the Spring of 1914 and Dr. Bissett opened a practice in Windsor, prompted in part by a family tradition that Bissett boys should be educated at King's Collegiate School. A son of a lineal ancestor, the First Rector of Trinity, St. John, was one of the first students enrolled at King's College School when it opened in 1787. An uncle, Dr. Henry Bissett, attended the school in the 1860's, later graduating from Harvard University and both Dr. Bissett's sons, Harold McKeen Bissett, Windsor barrister, and Lieutenant Victor E. Bissett, R.C.N., are "Old Boys" of the School.

Dr. Bissett's early mining community experience imbued him with an interest in public health as a prevention of epidemics and he was one of the pioneers in Nova Scotia in advocacy of comprehensive health measures. In his practice he carried on that ideal, being for 25 years Medical Health Officer for the town. His training under outstanding specialists in various fields of medicine qualified him as an authority on diagnosis, and his unusual skill in this respect was appreciated by fellow physicians.

Dr. Bissett is survived by his wife, and sons, and brothers Fred. W. of Halifax, George, of St. Peters and Alfred, William and James of Vancouver. Mrs. Mary Durand, Halifax, is a sister. An uncle, the late Charles Bissett, was for years Local Member for Richmond County.

Dr. Rodriguez Bourgon, of Montreal, died May 5 after a prolonged illness, in his 44th year.

Dr. Bourgon was born in St. Telesphore de Soulanges, the son of Leon Bourgon, and was educated at St. Mary's College and University of Montreal (1923).

He was intern at Hotel Dieu Hospital, and later moved to Northampton, Mass., State Hospital, as medical assistant. In 1924 he was clinical assistant at St. Antoine Hospital in Paris, where he served three years, and was later foreign medical assistant at the University of Klunick in Budapest as well as the Gynæcology clinic at Lourich, Budapest. Dr. Bourgon was prominent in medical circles there, obtaining his membership in the postgraduate, A.M.A., of the University of Budapest, being elected president of the American Medical Association of Budapest and Vienna.

Besides being resident surgeon at St. Jeanne d'Arc Hospital in Montreal, he was a surgeon at St. Jean de Dieu Hospital, governor of the Medical College of the Province of Quebec, and head surgeon at Notre Dame de la Merci Hospital.

Dr. Harry A. Boyce, of Kingston, Ont., died April 8, 1943, aged 65. He graduated at Queen's University in 1907 and M.R.C.P., London. He took postgraduate work in London, Vienna, Berlin and was superintendent

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of the Kingston General Hospital for 7 years. He held the following offices at various times: Lecturer in medicine at Queen's University, Past-President of the Canadian Hospital Association, Past-Secretary of the American Hospital Association, Past-President of the Kingston and Frontenac Medical Society and Past-Member of the Executive of the Ontario Medical Association.

Dr. Charles A. Eggert, of Vancouver, a pioneer physician of Prince Rupert, B.C., died on March 8, 1943. He was born in 1879 and a graduate of McGill University (1897).

Dr. Eggert was Swiss by birth but had practised in Prince Rupert from the early days, having removed from Atlin. He retired a few years ago. He is survived by his widow.

Dr. Alfred Johnston, of Cookshire, Que., died in Toronto, at the home of his daughter, Mrs. Carl Fraser, on May 6. He was a graduate of McGill University in Medicine (1901) and of Morrin College, Quebec (in Arts). He was 71 years of age.

Dr. Johnston had practised medicine for 32 years at Cookshire. He retired about six years ago, and since then has been living with various members of his family.

He is survived by three sons, F/O E. Wyatt Johnston at the R.C.A.F. Hagerville Station, Ont.; Lieut.-Col. Teryl Alfred Johnston, General Staff Headquarters, Ottawa; and Major Jack W. Johnston, now overseas, and one daughter, Mrs. Fraser, formerly Miss Carol A. Johnston, of Toronto, and several grandchildren. His wife, formerly Miss Jean Bracken, of Leeds, Que., died 10 years ago.

Dr. Alan Ernest McKibbin, of Oshawa, died on May 1. He was born in Chelsea, Que., in 1887, a son of Rev. R. V. and Emma (Church) McKibbin. On returning from overseas in 1918, he became attached to the staff of Whitby Military Hospital and entered private practice there in 1919. Dr. McKibbin served as a Captain in the R.A.M.C. in the last War.

He is survived by his widow, formerly Margaret Beattie Somerville; a daughter, Peggy; a son, Hugh David; a sister, Mrs. George Fawcett, and a brother, Reginald, of Georgetown.

News Items

Alberta

Some criticism has been heard about the plan of Federal Health Insurance which places the need of specialist's treatment in the hands of the general practitioner. It is felt that the privilege of going directly to an eye, ear, nose and throat specialist should be permitted, and the patient should not be obliged to go first to his family physician.

Again the Alberta Division and the Medical Faculty have held a most successful "Refresher Course" at the University, in Edmonton. A special effort was made to have a program that would appeal to the medical members of the armed forces as well as the American medical men now in this province in connection with the road development in the northern portion. Dr. L. T. Coggeshall, Professor of Epidemiology, School of Public Health, Michigan University, and Dr. E. E. Osgood, Associate Professor of Medicine, University of Oregon, Portland, were present and rendered great assistance to the successful meeting. The following officers from the forces also contributed much to the program: Lt.-Col. Kenneth Hamilton, R.C.A.M.C.; Lt.-Col. J. D. Adamson, R.C.A.M.C.; Lt.-Col. Gordon Fahrni, R.C.A.M.C.; Major W. Somerville, R.C.A.M.C.; Major M. B. Perrin, R.C.A.M.C.; Major O. Rostrop, R.C.A.M.C., Wing Commander F. F. Tisdall, R.C.A.F.

The following members of the University staff also rendered valuable services on the program: Drs. R. M. Shaw, H. H. Hepburn, Harold Orr, D. G. McQueen, F. H. H. Mewburn, Walter Anderson, A. R. Munroe, R. G. Huckell, M. R. Levey and I. R. Bell.

Dr. A. E. Archer, President of the Canadian Medical Association, gave an address on the working of the Medical Procurement and Assignment Board.

Local men were present from all parts of the Province, from Grande Prairie in the north to Medicine Hat and Lethbridge in the south, and from many places between.

The Board of Directors of the Alberta Division, Canadian Medical Association, held a meeting at a noon luncheon during the "Refresher Course" and laid plans for the district meetings which are to be held during the summer. They also planned for the Annual Convention which will be held in Calgary about the middle of next September.

It is doubtful whether the Government will be able to arrange for the Travelling Health Clinic to visit the outside districts of the Province this year, the exigencies of the war having its effect on the planning.

The matter of life insurance examination has been taken up by the Council of the College and a special letter has been sent to all the members of the profession, urging them to keep faith with the regular insurance companies and do no examinations for less than the agreed on fee of $5.00.

Dr. John A. Munroe, of Strathroy, Ontario, has joined the Associate Clinic of Calgary.

Dr. J. J. Diner, of Winnipeg, has become associated with Dr. J. C. Shillabeer, of Wetaskiwin.

Dr. Stuart M. Scott, of Morden, Manitoba, has joined the staff of the Federal Department of Defence and National Health at Edmonton. G. E. LEARMONTH

British Columbia

The Care of Old-age Pensioners.—We reprint the following extract from the *Bulletin of the Vancouver Medical Association* (April, 1943). It deals with a point of great interest to the profession generally, although at the moment one Province only is concerned. Nothing illustrates more clearly the ramifications which grow out from a scheme so far reaching as Health Insurance promises to be.

"The medical profession of this Province has been much disturbed recently, and rightly so, by the action of governmental authorities with respect to old-age pensioners. For quite a while we saw reports in the daily press to the effect that these persons were to receive free medical attention in addition to the living allowance they now have. This seemed praiseworthy and even generous. But while the motive may have been sound, the execution of the scheme was not so good. Without any formal consultation of the medical profession, or in any attempt to obtain their views on the matter, the Government went ahead and informed each of these pensioners, by a circular letter, that from now on they could go to the doctor of their choice and obtain free medical treatment. A card was given each of them, which the doctor was to sign, signifying thereby his willingness to assume the care of the pensioner.

"This was, as we have said, very generous of the government—but, after all, it is easy to be generous with other people's time and money—and we of the medical profession rather resent this action. The basis of payment has not yet, we understand, been formally stated: we question if any decision has been made at all: and in any case, our opinion was not

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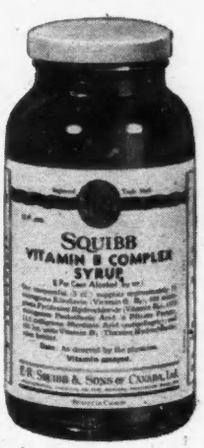

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asked, as a profession, nor our permission obtained, before our services were so generously given away. As far as we can make out, the general idea is to use the relief rate as a basis.

"There are several points here to be considered, apart from the serious objection raised above, that we have not consented to any plan. First, the relief rate, as well as the whole plan of medical assistance given to patients on relief, should not and must not be used as a standard for treatment of such groups as old-age pensioners. Relief assistance was a temporary expedient, and we hope it will disappear. Old-age pensioners and mothers' pensioners will probably always exist, and a permanent policy should be worked out for their care. And it should be worked out by full conference and consultation between the parties concerned. The organized medical profession through its duly constituted Council and Economic Committees, should be the ones to review this whole question and decide on what would constitute a fair scheme, and no individual doctor should agree to assume this work until this is done.

"Secondly, the relief medical scheme is a very poor one indeed. It gives a poor, inadequate service—and we would think it disgraceful that such a medical service should be all that can be given to old-age pensioners. These people are old, often ill, often helpless. They require a lot of care: and an adequate, efficient scheme, including hospitalization, should be worked out for them. Anything less than this would be quite inadequate.

"Lastly, we are concerned for the reason that if this is to be the attitude of governmental authorities towards pensioners, the indigent, etc., then there is grave reason for us to consider what sort of place in a health insurance scheme, which we now see in the near future, is to be assigned to these unfortunates. As a profession, we have again and again formulated our ideas as to how they should be taken care of and this miserable, half-baked scheme is certainly a long way from what we feel is right. We hope our leaders will take cognizance of all this, and that they will take a definite and firm stand in the matter. We urge all medical men not to act as individuals, but to refer all such schemes and suggestions to their regularly constituted representatives."

Manitoba

At a recent meeting of the finance committee of the Winnipeg City Council a recommendation that city-owned property in the vicinity of the General Hospital be withheld from sale was passed on to the properties committee for favourable consideration. Mayor Garnet Coulter said he expected a great post-war medical centre at the site of the General Hospital. It is possible that the Children's Hospital may be moved to a site close to the General Hospital and Medical School. A committee has been named to lay plans for the creation of a medical centre in that neighbourhood.

In the present assizes when a trial was held on a charge of procuring abortions, the court expressed the opinion that the crown, in future, in prosecuting this class of offence, should bring before the court not only the person who performs the illegal operation, but also those who seek medical aid to avoid the consequences of their earlier embarrassment.

Applications are being received for the post of medical director of Manitoba Medical Service.

Dr. A. T. Pincock has been appointed Associate Psychiatrist at the Winnipeg General Hospital and Dr. Brian Bird, Assistant Psychiatrist.

The annual meeting of the Canadian Medical Association (Manitoba Division) has been set for September 22, 23, 24 at the Royal Alexandra Hotel, Winnipeg.

The Manitoba Government has announced that it will provide at least six bursaries for medical students outside of Greater Winnipeg. They will be known as the Dr. David A. Stewart Memorial Scholarships. The bursaries will be advanced in the first instance as loans. Because the plan was authorized mainly to relieve the shortage of doctors in rural districts, students to whom awards are made will be asked to sign an agreement with the government when they graduate to practise in rural Manitoba or accept a position with the department of health. For each year so spent one-sixth of the loan will be remitted. The maximum amount of each bursary will be $2,150.00 of which $150.00 will be contributed by the University of Manitoba and $2,000 by the Manitoba Government.

ROSS MITCHELL

New Brunswick

The regular monthly meeting of the Saint John Medical Society was held on April 22. Dr. H. A. Farris was chairman and Dr. T. E. Grant completed his presentation of the subject "Fluid and electrolyte balance".

Dr. N. Skinner has returned from a two weeks' postgraduate study in Boston and New York. Dr. Skinner has recently been made a Fellow of the American College of Physicians.

The executive committee of the New Brunswick Medical Society held their spring meeting in Saint John on April 14. The president, Dr. H. E. Britton, presided. Dr. S. W. Burgess, of Moncton, was nominated for a senior membership in the Canadian Medical Association. A considerable discussion on allowances for motor car expenses for income tax purposes resulted in the motion to request the Canadian Medical Association to discuss with the Federal Government the possibility of raising the percentage of car expenses allowed as a deduction from 75 to 85% as there is now no pleasure driving.

Another request forwarded to the Canadian Medical Association for advice and action dealt with postgraduate and convention expenses. It was pointed out that at present such meetings are largely business, carried on in the interest of the profession at large, and to the benefit of the whole profession and of the whole country's population. It was felt that such expenses to such conventions should be considered business expenses and as such deductible for income tax purposes.

The executive committee of the New Brunswick Medical Society comprises the local divisional advisory committee of the C.M.P.A.B. and it received and approved the report on the manpower survey prepared by Major W. O. MacDonald, which was subsequently presented at the meeting of the C.M.P.A.B. at Ottawa. It was decided that in spite of difficulties, which include lack of hotel accommodation, the meeting of the New Brunswick Division would be held in Moncton on July 13 and 14.

Dr. Arnold Branch, Provincial Pathologist, has recently been granted membership by the American Board of Pathology.

Promotions in the R.C.A.M.C. Reserve Unit, the 2nd 14th Field Ambulance at Saint John show Captain A. L. Donovan promoted to a majority and Lieutenants J. R. Nugent, R. J. Collins and L. McPherson promoted to be captains.

A. STANLEY KIRKLAND

DIPHTHERIA TOXOID AND PERTUSSIS VACCINE

(COMBINED)

The death rate from diphtheria and whooping cough is highest among children of pre-school age. It is desirable, therefore, to administer diphtheria toxoid and pertussis vaccine to infants and young children as a *routine procedure*, preferably in the first six months of life or as soon thereafter as possible.

For use in the prevention of *both* diphtheria and whooping cough the Connaught Laboratories have prepared a combined vaccine, each cc. of which contains 20 Lf's of diphtheria toxoid and approximately 15,000 million killed bacilli from freshly-isolated strains (strains in Phase 1) of *H. pertussis*.

CONVENIENCE

The combined vaccine calls for fewer injections, and, in consequence, the number of visits to the office or clinic may be considerably reduced. It is administered in three doses with an interval of one month between doses.

EFFICACY

Studies have shown that the combined vaccine is an effective immunizing agent against both diphtheria and whooping cough.

DIPHTHERIA TOXOID & PERTUSSIS VACCINE (COMBINED) is supplied by the Connaught Laboratories in the following packages:

Three 2 cc. ampoules—For the inoculation of one child

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Ontario

The College of Physicians and Surgeons of Ontario held its 78th Annual Meeting of Council on April 14, 1943. Officers for 1943-44: President—C. S. Sanborn, M.D., Windsor; Vice-president—G. L. Macdougall, M.B., Whitby; Registrar-Treasurer—R. T. Noble, M.B., Toronto.

The Council reaffirmed its former attitude towards the National Health Insurance that the College is particularly interested in the effect a Health Insurance Bill may have directly or indirectly on medical education. Medical standards of education and the maintenance of professional efficiency are matters which effect the welfare of the general public and are the direct responsibility of the College. Direction was given to the Committee to co-operate in every way possible in giving assistance to the Committee of Seven in making suggestions towards the preparation of the Health Bill.

Another matter of interest to the profession in Ontario is the appointment at a special conjoint meeting of the Council of the College and the Board of Directors of the Ontario Medical Association of the following Committee: O.M.A. Members.—Dr. H. D. Logan, Lindsay; Dr. William Magner, Toronto; Dr. H. M. Torrington, Sudbury. College Members.—Dr. M. H. V. Cameron, Toronto; Dr. A. Moir, Peterborough; Dr. John R. Stewart, Toronto.

A Progress Report was received from this Conjoint Committee *re* Organization and it was unanimously carried by Council that:

"The Council of the College of Physicians and Surgeons of Ontario, after having carefully considered the report of the Conjoint Committee *re* Organization, wishes to express its appreciation of the work done by the Committee and in its desire to more fully co-operate would recommend further study of the report with the Board of Directors of the Ontario Medical Association at some convenient time after its annual meeting in May.

"This would seem to be desirable as all members of the Committee of Six would be present and conjointly the College and the Ontario Medical Association could decide what further action is best to take in regard to the matter in question." ROBERT T. NOBLE, *Registrar.*

A small collection of rare books has been gathered in Queen's University as the beginning of a memorial to the late Professor Gibson. This tribute to an eminent scholar will appeal to the alumni of Queen's because of its singular fitness and will undoubtedly grow into an important and valuable addition to the library of the University.

Another gift to the Medical Library of Queen's came from Dr. Henry Sigerist, Editor of the *Bulletin of the History of Medicine* through Dr. Frederick Etherington, Dean of the Faculty. The donation numbers 75 items of which 32 are by Dr. Sigerist himself. At the centenary of Queen's in 1941 Dr. Sigerist gave one of the principal lectures and was granted the LL.D. degree.

Lt.-Colonel Howard McCart who has been with No. 15 Canadian General Hospital in England for the past three years, has been recalled to resume his appointment in the Department of Otolaryngology, University of Toronto.

The Academy of Medicine of Toronto has completed another year of activity. All reports to the annual meeting on May 4 were encouraging. The membership now stands as 1,204, of whom 279 are on active service with the armed forces. The Library Committee reported a gain of 614 volumes during the year bringing the total number of books to 30,960. Duplicate journals of recent date were sent to military camps and hospitals outside the city and 85 books sent through the International Y.M.C.A. to prisoners of war in Germany. The report also contained a tribute of deep appreciation of the services of the late Dr. Jabez Elliott, who had served 35 years on the committee.

The officers for the coming session are: *President*—Dr. Robin Pearse; *Vice-president*—Dr. J. Z. Gillies; *Secretary*—Dr. H. E. Hopkins, and *Treasurer*—Dr. Roy Thomas. The retiring President, Dr. Samuel Johnston, installed his successor.

On April 17 a complimentary dinner was tendered Dr. Norman Shenstone by about fifty of his colleagues in Toronto. Dr. Shenstone had recently received an Honorary Fellowship in the Royal College of Surgeons of England in recognition of his contribution to surgical science and, in particular, of his outstanding work in thoracic surgery. Tnis rare distinction was granted many years ago to the late Professor I. H. Cameron and, more recently, to the late Sir Frederick Banting.

Dr. Joseph Sullivan has been appointed Consultant in Otolaryngology with the honorary rank of Wing Commander in the R.C.A.F. He is attached to No. 6 School of Aviation where he lectures on his subject and is engaged in research work on the special problems of aviation as it affects the ear. Dr. Sullivan has already done brilliant work on nerve transplantation in facial nerve injuries and in the operative treatment of deafness due to sclerosis.

The Annual Meeting of the College of Physicians and Surgeons of Ontario was held in Toronto on April 14 and 15. No serious matter had come before the discipline committee during the year. Two or three names were readmitted to the register. Besides routine matters the question of amending the Medical Act of Ontario to allow closer co-operation with the Ontario Medical Association was discussed. The report of a joint committee of the two bodies was received and referred back for further consideration by the Councils of the two bodies concerned. Tentative approval was given to the modification of the regulation calling for six years of 30 weeks each in the undergraduate course. Should the universities rearrange their courses so that five years of 36 weeks are provided the college would probably accept the new arrangement. In view of the increase in volume of the business of the Council of the College it was decided to hold two sessions each year instead of one. This will lessen the work of the Executive Committee, which was called four times since the annual session of 1942. Dr. C. S. Sanborn, of Windsor, was elected President and Dr. G. L. Macdougall, of Whitby, Vice-president. The retiring President, Dr. Archibald Moir, of Peterborough, gave the presidential address.

Lt.-Col. Henry Argue of headquarters M.D. 2 has been appointed Senior Medical Officer of the Canadian Contingent in Newfoundland and leaves immediately for his new post. M. H. V. CAMERON

Quebec

Les Journées Médicales de la Société Médicale de Montréal auront lieu les 14, 15, 16 et 17 juin 1943 sous la présidence d'honneur de l'Hon. Henri Groulx, Ministre de la Santé et du Bien-Etre Social. Les séances, qui comportent toutes des exhibits scientifiques auront lieu à l'Hôtel-Dieu, à l'hôpital Général de Verdun, à l'hôpital Ste-Justine et à l'hôpital Notre-Dame. L'nscription est gratuite pour les membres et leurs invités.

A le Semaine de Pédiatrie de l'hôpital Ste-Justine,—24 au 29 mai—sous la direction du Pr. Gaston Lapierre, les sujets suivants seront traités: l'épilepsie infantile; les dermatoses infantiles; le rachitisme; les lésions chirurgicales congénitales du nouveau-né; les conquêtes récentes sur le front médical; la syphilis du nourrisson; les maladies du nouveau-né; l'hygiène de la première enfance et de l'âge scolaire; le problême amygdalien et le problême endocrinien à l'école.